Clinical Medicine

February
1960

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FEBRUARY, 1960 *Volume 7, Number 2*

editorial

original articles

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- in sinusitis and postnasal drip
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1. Fabricant, N. D.: E.E.N.T. Monthly *37*:460 (July) 1958.
2. Lhotka, F. J.: Illinois M. J.: *112*:259 (Dec.) 1957.
3. Farmer, D. F.: Clin. Med. *5*:1183 (Sept.) 1958.

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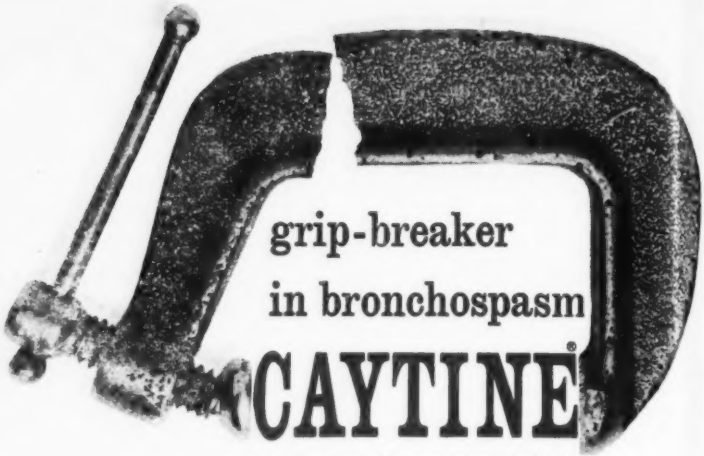

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(1) Leslie, A., and Simmons, D. H.: Am. J. M. Sc. *234*:321, 1957. (2) Settel, E.: Am. Pract. & Digest Treat. *8*:1249, 1957.

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Detection of Abnormal Behavior Patterns by EEG

JAMES M. NORTHINGTON, M.D., *Editor-in-Chief*

►*Electroencephalography, a valuable diagnostic aid in treating diseases of the nervous system, is also being shown helpful in detecting criminal types before their social behavior patterns manifest themselves. EEG studies among twins indicate the possible detection of schizophrenia and homosexuality.*◄

In a recent issue of a foreign journal, an eminent teacher and practitioner of psychiatry[1] has set forth foundation information on the electroencephalogram in relation to abnormal behavior. It is my hope that this relation, discussed by this evidently highly qualified authority, will help to achieve a better understanding of neuro-psychiatric articles.

In a random sample of the adult population, EEG wave forms of 85% will be relatively consistent, uniform, and similar. Some 15% of the records will, however, contain significant abnormalities which can be divided into two groups:

1. Those which can be directly correlated with some damage or abnormality of brain structure, e.g., tumor or abscess in the brain.

2. Those which are related to disturbance of function without demonstrable structural disorder.

This latter category can again be subdivided into abnormal patterns associated with specific clinical disturbance of brain function, such as the various forms of epilepsy and abnormal patterns which, because they have not been regarded as corresponding to any specific disorder of behavior in the past, have been noted as abnormal without being recognized as specifically significant. These non-specific abnormalities make up a large proportion of the 15% of abnormalities seen in the population as a whole. They include changes in the rate and rhythm of the brain waves of a

1. Stafford-Clark, D., *Brit. M.J.*, 2:1199-1204, 1959

kind which are normal in infancy but become progressively less frequent as the brain matures.

Fortunately, an exceedingly significant question concerning this field of research was answered simply by reviewing the history and personal circumstances of each individual in terms of the crime with which he or she was charged. In this way it was possible to make a number of separate clinical categories, each of which could be studied separately in terms of the EEG records of the particular group.

One of these categories included accidental murderers, persons who had been involved in action resulting in loss of life while already engaged upon the commission of a felony, and who, while evidently criminal, were certainly not to be regarded as wilful murderers. A second category was that of the deliberate, motivated murderer; persons who had committed murder for reasons which they and everyone else concerned could relate to the basis of the crime. One of the two remaining categories is that of motiveless murderers, who had committed sudden explosive acts of violence causing the death of another person (for no reason which they or anyone else could establish); and persons who were recognizably insane at the time of the killing.

The group of murderers whose crime was regarded as incidental or even accidental in the course of the commission of another felony showed a 25% incidence of EEG abnormality, the same as that of the prison population as a whole. In those who had committed a murder under the stress of great provocation, and were to this extent clearly motivated, the proportion of abnormality was roughly 17%, considerably below the average for the prison population as a whole and not very much above that of the ordinary population chosen at random. In the apparently motiveless murderers (persons who committed an act of violence without any kind of provocation other than perhaps the immediate stress of sexual excitement, resentment, or exhaustion), the percentage of abnormality was 73.

It should be remembered that these are only percentages of abnormality within a group. One-quarter of even the motiveless murderers had normal EEG records. The tendency to commit an apparently motiveless act of extreme violence nevertheless seems to be linked with instability and immaturity of brain function, which can be objectively recognized and recorded. It is clear that research in this

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direction still represents little more than a groping after the most shadowy outlines of truth. This groping, however, may be rewarded by increasing definition as results (in terms of clinical study correlated with increasingly accurate measurement of findings) are pooled and interpreted.

Relatively extensive follow-up studies in which the life-history of each of a pair of identical twins has been compared with that of each of a pair of non-identical twins (when one of each pair has suffered from schizophrenia or has developed homosexual traits), have given the following results:

In a large series of identical twins, one of each pair having schizophrenia, over 80% of the other twins developed this illness (this rate persisting even when both twins had been separated from birth). In non-identical twins the concordance rate was no more than 15%, about the average expectation rate for siblings of a schizophrenic.

In identical twins where one twin has developed homosexual behavior, the other twin has been found to develop it in 75% of all cases; whereas the concordance rate in non-identical twins is about 5%—no higher than that estimated as the incidence of homosexual tendencies in the population as a whole.◄

Pruritus: Adjunctive Management with Bath Oil

A clinical evaluation of bath additives for a period of 2 years demonstrated the effectiveness of a bath oil combination containing a dewaxed, oil-soluble keratin-moisturizing fraction of lanolin, a non-ionic emulsifier (polyethylene glycol laurate), mineral oil and a synthetic perfume of low sensitivity (alpha-KERI Oil), as an adjunct in the treatment of senile and other forms of pruritus. Patients are instructed to soak from 5 to 20 minutes in a tub of lukewarm water containing ½ to 1 ounce of the oil, in this way cleansing the skin and leaving a film of emollient, moisture-retaining oil on the keratinous layers. The baths produced good results in most cases of senile pruritus in 182 patients and of pruritus due to other dermatoses in 772 patients. They are especially recommended to supplement use of emollient creams and of large doses of vitamin A where extensive areas are involved.

James, A. R. P., *Southwest. Med.*, 40:384-385, 1959.

original article

Differential Diagnosis of Severe Neurologic Deficit in Children

CHARLES M. POSER, M.D.,* *Kansas City, Kansas*

►*Pediatric neurology is beset by more emotional factors than any other branch of medicine. Heredity and parental attitudes are but a few of the complications. An intensive study into all aspects of the case is imperative, not only because of the corrective measures to be taken, but because of the consequences.*◄

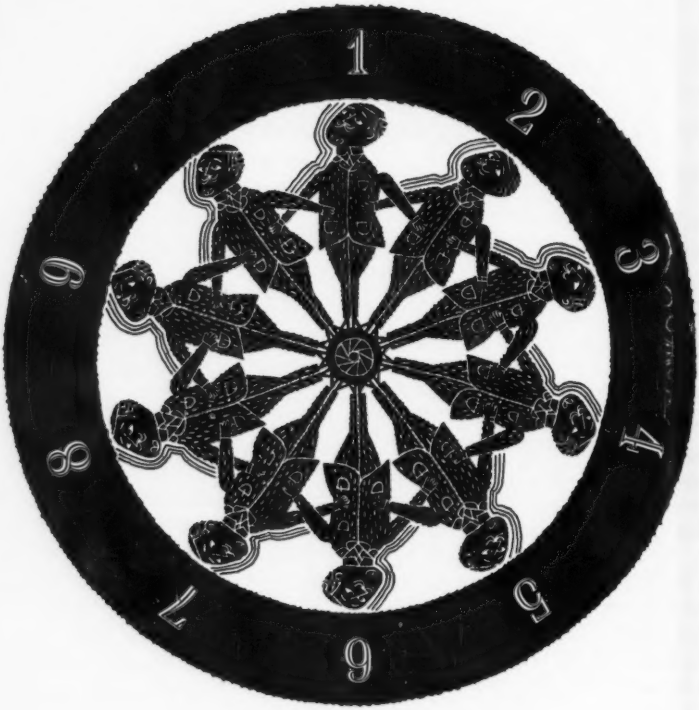
For the practitioner of medicine there is probably no more complex task than the diagnosis and management of neurologic disease in the infant and child. A number of non-medical problems are closely connected to, and perhaps responsible for, this complexity. Parents may be poor observers or unreliable historians; information concerning the pregnancy and the delivery may be unavailable; in many cases there are deep-seated feelings of guilt on the part of the parents.

The possible etiologic agents causing neurologic deficit in childhood run the whole gamut of traumatic, metabolic, infectious, vascular, neoplastic, and congenital diseases. Naturally, the physician must try to determine the etiology of the disturbance, but in addition, and equally important, he must try to determine the time when the responsible lesion became active.

Examination Findings Apt to Mislead

The neurologic examination of the infant and the young child is both difficult and easy. It is difficult in that the physician often cannot obtain the child's cooperation in eliciting the necessary symptoms and signs. It is easy in that a great deal of important information can be obtained from simple observation of the child. In such an examination he should remember the tremendous value of the developmental landmarks which are the best measurements of the status of the child's nervous system. The first, and often the only, indication of

*Associate Professor of Medicine (Experimental Neurology) University of Kansas Medical Center.



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References: **1. Menger, H. C.: Clin. Med. 4:313 (Mar.) 1957. 2. Seal, J. C.: Eye Ear Nose & Throat Month. 39:736 (Sept.) 1960.**

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neurologic deficit is manifested in the child's failure to reach the developmental landmarks at the proper time. A word of caution is indicated in the interpreting of these landmarks, since the ages set down in textbooks as those by which various performances should be achieved are simply average figures. A child who does not sit up even at the age of 8 months, rather than 6 months, is not necessarily retarded.

One great difficulty arises in attempting to differentiate between progressive and non-progressive disease, as well as between true progression and pseudo-progression. In many instances the child's deficit becomes more evident as he grows. This increasing disability may be caused by progression of the disease process. More often than not, however, it is simply due to the fact that the growing child makes more and more demands upon his basic mental and physical endowment. If this endowment is deficient, it cannot meet the new requirements, and thus the disability appears to be increasingly greater. Many children do not manifest their neurologic deficit until later, when the so-called higher functions should be developing, and attention is first drawn to the deficit by their failure to develop speech. In such cases the neurologic lesion was present all the time but did not become manifest until later.

History Should be Extensive and Thorough

A thorough and extremely detailed history of the pregnancy, delivery, and early infancy and childhood is the prime essential. We know that German measles in early pregnancy is prone to cause malformations of the central nervous and cardiovascular systems in the children born of these pregnancies. There are probably other such factors, perhaps x-radiations, the influence of which is still poorly understood. A great deal of caution must be exercised in interpreting events at the time of birth before assigning an etiologic role to them. Thus a precipitate labor may be much more harmful than a prolonged one. The use of forceps has been considered responsible for many more birth injuries than it can really be held accountable for. It is easily forgotten that malformed fetuses are often the cause of a difficult delivery rather than its result. Anoxia or intracranial hemorrhage, either spontaneous, the result of intra-uterine conditions, or the result of rare obstetrical trauma, may give rise to conditions which are indistinguishable from those resulting from agenesis of various parts of the brain.

Ambiguous Terms Are Confusing

Any disease which is present at birth is described as "congenital," according to many standard dictionaries. Unfortunately, the word "congenital" is often used loosely and interchangeably with "familial" or "hereditary," both of which mean quite different things. To be truly hereditary, a disease must be genetically determined at the time of conception. It must be the result of the interaction of genes present in the sperm and ovum, unaffected by environment. Such a disease need not necessarily be familial, since according to the laws of heredity, one of the offspring may be afflicted and others may not be. The mother's genetic make-up may also have an indirect effect on her offspring. For example, diabetes probably represents a hereditary disease. The fetus of a diabetic mother may be harmed by the diabetes influencing intra-uterine conditions. Its development will have been determined by genetic factors, but only indirectly.

Hereditary disease may be familial, but not all familial disease is truly hereditary. The fact that the same disease is seen in siblings is not proof that it is inherited or genetically determined. Kernicterus, caused by Rh incompatibility, may be familial, as may any other disease which is the result of environmental factors affecting intra-uterine life, if such factors remain operative in more than one pregnancy.

These semantic clarifications have practical applications, since they must be kept in mind when counseling families about further pregnancies following the birth of a defective child.

Examiner Must Be Alert to Detail

Even though it may be extremely difficult to diagnose neurologic disease at birth, there are certain conditions that must be recognized. An infant who has convulsions should be suspected of having a subdural hematoma, even if no history of trauma can be obtained. The characteristic configuration of premature closure of the cranial sutures can be recognized at birth and treated by surgery. The cretin and the mongol can be identified early. Proper therapy should be instituted in the former, while the latter should be observed for a long time within the family group before institutionalization is suggested. Not all mongols are at the idiot level, and certainly not all of them need to be institutionalized. Hydrocephalus must be taken care of immediately with neurosurgical procedures so that there may be a good prognosis for the condition.

Not All Symptoms Due to Central Nervous System Lesions

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lems facing the physician in dealing with the "retarded" or "crippled" child is to determine if the disability is the result of a lesion of the central nervous system. A child who has muscular dystrophy will be late in standing up and walking; a child who has myasthenia gravis will not suck well and will fail to gain weight and develolp normally; a child with congenital dislocation of the hips will not walk; while a child's failure to develop bladder control may be caused by a spinal cord disease such as diastematomyelia rather than a psychiatric reason. Psychiatric factors are only too often glibly invoked in children who have difficulties. Because of this they are denied neurological investigation which may lead to correction or cure. This is especially true of children with certain forms of borderline epilepsy which are often manifested by bizarre episodic emotional disturbances. Electroencephalograms often reveal the true epileptiform nature of the condition, and proper use of anticonvulsant medication results in control of the condition.

Consider Effect of Diagnosis on the Patient

A dangerous tendency today in dealing with children with neurologic deficit is to classify them as victims of "cerebral palsy" or as "mentally retarded" instead of attempting to make an accurate diagnosis. There is a final and definitive quality in those terms which blinds the users to the fact that they are meaningless. Unfortunately, these terms also close the door to further investigation. Many of the children who are diagnosed as "mentally retarded" are deaf children who for obvious reasons were never able to learn to speak. Pseudo-retardation caused by deafness, blindness, or some chronic illness must be differentiated from true retardation. It is no longer sufficient to classify the slow child in terms of his I.Q. An attempt must be made to discover the nature of the disease causing the retardation. We now know that several inborn errors of metabolism which cause mental retardation, such as galactosemia and phenylketonuria, can be helped by dietary measures if they are instituted early enough. This puts a premium upon the need for early diagnosis following thorough investigation of the child.

Among children with "cerebral palsy" are seen a wide variety of disorders, both neurologic and other. Children with true orthopedic disturbances are easily differentiated from those with diplegia due to spinal cord disease, but those who have early dystonia musculorum deformans are often

erroneously and harmfully treated for club foot.

Accurate Diagnosis the Key to Best Treatment

Certainly the most important reason for making any diagnosis is so that effective treatment may be instituted. In neurologic disease of the infant and child, the treatment may be physical, dietary, or pharmaceutical. Children with severe epilepsy often show evidence of mental deterioration. This deterioration is not caused by the epilepsy itself, but results from the repeated episodes of head trauma and cerebral anoxia which accompany every convulsive seizure. It is these patients whom the alert physician can help most successfully. Control can be achieved in 75 to 85% of epileptic children by the judicious and early use of anticonvulsant medication.

We need to know a great deal more about the effects upon the central nervous system of various affections of infancy and childhood. We know, for instance, that the viruses causing the so-called benign exanthemata are all potentially neurotropic. Evidence has been presented that even in cases of uncomplicated measles or mumps, the central nervous system is affected sub-clinically. We also know that the central nervous system of the child is more delicate than that of the adult and cannot withstand as much in terms of traumata as can that of the adult. This applies especially to convulsions and points to the need of attempting to prevent convulsive episodes whenever possible. This should be borne in mind when dealing with children with febrile convulsions. More often than not, these are epileptiform and should be treated as such.

The proper way of arriving at the correct diagnosis in the case of the disabled child is to employ the team approach. The prime responsibility naturally falls upon the family physician who sees the child first and detects the abnormality. The pediatrician, the neurologist, the neurosurgeon, the orthopedic surgeon, the plastic surgeon, the radiologist, the physiatrist, the ophthalmologist, the otologist, the speech therapist, the psychologist and the psychiatrist are indispensable members of such a team. It is only after the child has been seen by all the appropriate members of the team, and after the simple but specific laboratory tests have been performed, that his ailment can be diagnosed and the necessary therapeutic measures instituted. The term "cerebral palsy" should be banned. It has brought too much hardship upon the children so designated and left too many con-

ditions undiagnosed under the misapprehension that "cerebral palsy" is a diagnosis.

Not All Symptoms Establish Encephalitis

Another diagnostic term which is applied too loosely is that of "encephalitis." The combination of fever, headache, and convulsions is not sufficient to justify this diagnosis. Many children who have an underlying epileptiform tendency will react with this syndrome to a simple upper respiratory infection or a gastro-intestinal disturbance. The diagnosis of encephalitis cannot be made without evidence of spinal fluid leukocytosis. In the same manner, not every child with a fever and a stiff neck has meningitis. Many small children with cervical lymphadenitis resulting from a throat infection will have a stiff neck. There is no more dangerous practice than immediately to start treating a child suspected of meningitis with all available antibiotics. If meningitis is suspected, spinal fluid should be obtained for diagnosis and isolation of the specific causative agent by smear and culture, before any antibiotic is given. Too often, the early antibiotic prevents identification of micro-organisms and the determination of drug sensitivity becomes impossible. When a spinal tap is indicated by the clinical signs and symptoms, it is a simple, safe procedure.

In dealing with a child who has severe neurologic deficit, and especially with his parents, certain points should be remembered. Many parents feel deeply guilty about what they consider the curse that the Lord has visited upon the fruit of their loins. This is, unfortunately, a frequent interpretation of the tragedy of the exceptional child. Too often parents concentrate all their affection upon the disabled child while neglecting their other children. Many times they even decide erroneously not to have any more children because the eugenic advice they were given was based upon an incomplete or incorrect diagnosis.

Home the Locus for Most Treatment

Institutionalization of children should never be coldly recommended except in cases where the child is so obviously malformed or defective that it is impossible to treat it while keeping it at home. In most instances, however, two criteria should be applied in planning a therapeutic program for retarded or neurologically deficient children after establishing as exact a diagnosis as possible. The first is related to potential response to training; the second, to the practical goal of

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References:
1. Fox, H. H.: Antibiotic Med. & Clin. Therapy 6:85, 1959. 2. Lubowe, I. I.: Antibiotic Med. & Clin. Therapy 4:81, 1957. 3. Murphy, J. C.: Rocky Mountain M. J. 55:53 (June), 1958. 4. Pace, B. F: M. Rec. & Ann. 51:370, 1957.

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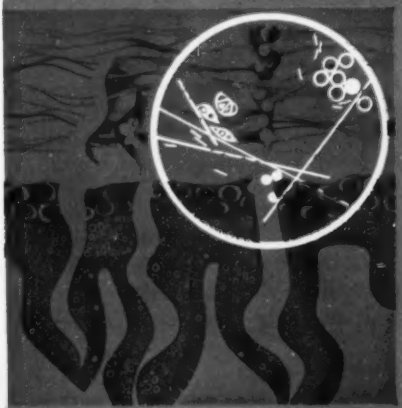

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therapy and training. It may seem harsh to tell parents at once that no amount of surgery, education, or physical and occupational therapy will make their child sit up or walk or talk; but surely it is even more heartless to wait to tell these same parents, several years and many thousands of dollars and hours of therapy later, that there is no hope for the child. Patients must be carefully selected for therapy, which should be based strictly upon medical considerations: the diagnosis and the child's potential, especially in terms of his mental endowment.

Consider All Factors of Every Case

Selection of patients must be made with the goals of therapy kept fully in mind, since the two are dependent upon each other. For some children, therapy and training must be limited to making the problems of institutionalization easier. For others, it must be gauged in terms of potential mental and physical ability. A good example of unrealistic rehabilitative effort is that of the persistent efforts usually made to teach a paraplegic child to walk. In many cases thousands of hours and dollars are spent in fitting orthopedic corsets and braces and training the child to use them, with the result that the child, painfully loaded down with heavy and ungainly apparatus, can—usually with the help of crutches—drag himself awkwardly from his wheelchair to the dinner table. This is *not* rehabilitation. In the course of attempting uselessly to stand and walk, the handicapped child has been denied the training that could have been achieved more realistically by confining him to a wheel chair and utilizing to the utmost his upper extremities which are now encumbered by crutches. In other areas such as schooling, standards are often too rigid and unrealistic. The goal should be to make the individual self-supporting to the degree that his intellectual endowment allows.

There is nothing particularly mysterious about the nervous system. As in all other branches of medicine, correct diagnosis achieved by all possible methods is the first requisite before treatment can be envisaged. In dealing with the neurologic problems of children, one of the main difficulties is a semantic one. Too many classifications are outmoded or overly comprehensive, too many terms are used loosely and thoughtlessly. Neurologists will accomplish a great deal by making new definitions and learning how to use them properly.

Each child with neurologic disease or deficit has a specific problem that cannot be solved simply by labeling it "cerebral palsy" or

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"mental retardation." The problems of treatment and eventual rehabilitation are so closely tied to those of diagnosis that the situation must be taken as a whole by the physician who is responsible for the child's general health problems.◀

Prophylactic Use of Ergometrine

Although prophylactic use of ergometrine in the second stage of labor reduces the incidence of post-partum hemorrhage, many believe this results in an increased rate of manual removal of the placenta. Of a series of cases, those treated with ergometrine in this manner showed a noticeably greater decrease in the incidence of post-partum hemorrhage (without any alteration in the rate of manual removal of the placenta) than that shown by those not so treated. Prior to this prophylactic therapy 0.5 mg. ergometrine had been given intravenously with the birth of the anterior shoulder to patients with a history of post-partum hemorrhage, a hemoglobin of less than 10.4 gm./100 ml. at the onset of labor, those para 4 or more, those with hydramnios or multiple pregnancy, after an ante-partum hemorrhage or prolonged labor and if operative intervention had been necessary. Prophylactic treatment during the second stage in these indications consisted of administering 0.5 mg. ergometrine (together with 1,000 units of hyaluronidase) intramuscularly with the crowning of the head. The remainder of the patients were not given ergometrine unless undue bleeding occurred either before or after delivery of the placenta.

There was no increase in the manual removal rate when ergometrine was used prophylactically in the second stage of labor. In addition to saving blood, particularly in patients prone to post-partum hemorrhage, this use of ergometrine shortened the duration of the third stage without increasing the hazards to the mother. Although the placenta and membranes are occasionally trapped by the closing cervix when ergometrine is given during the second stage, practising the Brandt-Andrews maneuver (if necessary supplemented by the inhalation of amyl nitrite) can overcome cervical spasm so that the separated placenta can be delivered from the cervix or vagina.

Huntingford, P. J., *Brit. M. J.*, 2:1071-1959.

Use of Hydroxyzine-Theophylline-Ephedrine Combination for Relief of Asthma

BEN C. EISENBERG, M.D.,* *Huntington Park, California*

►*The combination of a bronchodilator, antihistamine, and tranquilizer brought encouraging results to 117 patients suffering from the wheezing dyspnea common to asthma. Moderate to excellent relief was experienced in 83 per cent. Control of the attack as well as long-term therapy was provided by oral dosage.*◄

The combination of ephedrine, a xanthine, and a mild sedative (usually one of the barbiturates) has in recent years constituted a fairly reliable and popular medication in the management of asthmatic patients. In these patients, ephedrine has been found to improve the vital and respiratory capacities, lessen the volume of residual air, and moderately improve expiratory reserve volume. The xanthine component (aminophylline or one of its analogues) is said to enhance the aforementioned brochodilating effects, though this has been open to question, particularly in the widely used 0.1 gm. dosage. Phenobarbital or another sedative is added to the combination to mitigate some of the undesirable side-effects of the other drugs, i.e., nervousness, tachycardia, tremor, increase in anxiety, and insomnia.

More recently, the barbiturate component has been replaced by an antihistaminic, which serves a double purpose: 1. provides some sedation, and 2. enhances the antiallergic action of the two other drugs. This paper is a report on preliminary clinical experience with a drug combination† consisting of ephedrine sulfate 25 mg., theophylline 130 mg. and hydroxyzine (Atarax) 10 mg.

I became interested in this new formula chiefly because of the inclusion in it of hydroxyzine, which has been used with clinical success as a tranquilizing

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†*Marax®, J. B. Roerig and Company*, (Div. of Chas. Pfizer & Co., Inc.) New York, N. Y.

agent. The effectiveness of hydroxyzine in allergy and the treatment of acute and chronic urticaria has been reported.[1,2] The drug is virtually devoid of toxicity in the therapeutic dosage range, the chief side effect consisting of occasional transitory drowsiness. No instance of toxicity exists in the world literature, after more than 5 years of clinical use.[3] Worth noting, in the treatment of asthma, are the secondary pharmacologic properties of hydroxyzine. The ataractic provides antihistaminic, anticholinergic, antispasmodic, and antiserotonin actions. These properties would appear to offer greater therapeutic benefits than the mere sedative action obtained from a barbiturate combined in one tablet with the two other conventional drugs for asthma.

The ideal oral anti-asthmatic preparation should be effective in controlling symptoms; produce minimal or no side effects; offer ease of administration; and not interfere in any way with the daily work or life pattern of the patient. Even were such an ideal drug available, it could not replace comprehensive management of the asthmatic patient, including specific allergy treatments for hyposensitization. However, the various combinations of drugs (such as the combination under discussion) do afford marked relief in a large number of typically allergic asthmatic patients, particularly if used prophylactically rather than only symptomatically.

Pharmacologic Aspects of Hydroxyzine

A brief review of the antihistaminic, anticholinergic, antispasmodic, and antiserotonin actions of hydroxyzine as related to allergic conditions, asthma, and emphysema follows.

ANTIHISTAMINIC: Hydroxyzine, in a dose of 10 mg. per kg. in guinea pigs, was completely effective against anaphylaxis and nearly so against histamine. The drug produced striking results in 15 of 17 patients who obtained complete relief from chronic urticaria of undetermined origin. The study demonstrated that the sedative property of the drug was not responsible for the anti-allergic action.[2]

ANTICHOLINERGIC: In experimental work, the antiacetylcholine faculty of hydroxyzine was shown by Hutcheon.[4] The relative anticholinergic activity of atropine and hydroxyzine was the same as for vagal blockade; an atropine-like site of action for hydroxyzine was indicated.[4]

1. Eisenberg, B. C., *Clin. Med.*, 5:897,1958.
2. Feinberg, A., et al., *J. Allergy*, 29:358,1958.
3. Cohen & Cohen, *J. Allergy*, 29:542,1958.
4. Hutcheon, D. E., Fourth Pan. Am. Cong. Pharm. & Biochem., Washington, November, 1957.

ANTISPASMODIC: In studies of the antispasmodic properties of hydroxyzine both *in vivo* and *in vitro*, hydroxyzine, administered intravenously in a dose of 5 mg. per kilogram to the anesthetized dog, effectively antagonized and blocked the spasmogenic actions of acetylcholine, histamine and posterior pituitary extract. Enhanced activity resulting from serotonin and reserpine was also blocked.[5]

ANTISEROTONIN: A challenging aerosol dose of serotonin was brought to the guinea pig in a concentrated strength which by previous assay was found to produce asthma in these animals in two minutes.[2] Prior to this challenge, hydroxyzine, 10 mg. per kg. was injected intraperitoneally. No sedative effects were noted. In sum, hydroxyzine was shown to be a long-acting, potent, antianaphylactic, antihistaminic, antiserotonin, and antiacetylcholinic agent; other tranquilizing substances possess the foregoing properties not at all or only in part. Pharmacologic justification for the inclusion of hydroxyzine in place of a barbiturate in the clinically accepted drug combination for asthmatic patients is ample.[2]

Materials and Methods

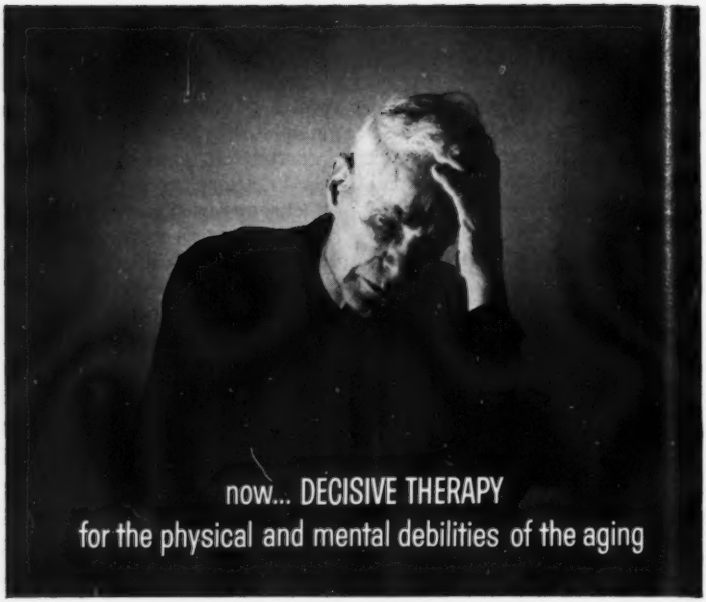
The patients selected were from a large group of asthmatics requiring various types of oral medication for relief of wheezing dyspnea. Most of this group was receiving specific allergy treatments for hyposensitization purposes but on occasion had to resort to drugs for relief of acute attacks, or resort to bedtime medication to prevent occurrence of nocturnal paroxysms of wheezing.

In all, 117 patients were given the drug combination. No double-blind studies were made. Previous medications used served as controls. Patients ranged in age from six to 75 years, with males and females in equal number. Patients for the most part adhered to a dosage schedule of 1 to 4 tablets daily as needed, or 1 to 3 tablets daily prophylactically. A few found 2 tablets at each dose necessary for relief. The group was followed for a period of 12 to 16 weeks.

Results

We have categorized the results into marked improvement; moderate improvement and no improvement. Marked improvement indicates complete relief of symptoms with the single or intermittent dosage; moderate improvement—fairly satisfactory but incomplete relief; no improvement—slight or no relief. Accordingly, 88 (76%) of the 117 patients studied obtained excellent relief; 9 (7%) moderate relief; 20 (17%) no relief.

5. Sherrod, T. R., *Toxicology & Applied Pharm.*, 1:162,1959.



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Side effects in 9 patients (8%) included nervousness and tachycardia—5 patients; epigastric distress—2 patients; drowsiness—2 patients.

Discussion

Since a new patient is frequently in the course of a severe asthmatic attack when the clinician first sees him, the first objective is control of the attack. Attainment of relief from the current attack involves measures to alleviate bronchospasm, mucous plugging, and local edema; and to provide emotional relief and ataraxia. Any existing respiratory infection must be treated with appropriate antibiotics. Prevention of recurrent attacks is next, although this ideal is seldom attained without appropriate specific therapy. Prophylactic administration of drugs is recommended because asthma may be considered a chronic disorder which is frequently present subclinically in these patients. Prophylaxis not only provides comfort for the patient but helps prevent irreversible pulmonary changes and damage. But symptomatic and prophylactic drug therapy must still be considered adjunctive to specific measures to overcome that patient's hypersensitivity to offending allergens by removing or immunizing against them.

Because long-term therapy is often required in these patients, hydroxyzine rather than a barbiturate with ephedrine-theophylline is of value. Hydroxyzine is neither a respiratory nor a cortical depressant. The drug is not habituating. Barbiturates given over a prolonged period to chronic asthmatics present obvious disadvantages. In the dosages used in standard anti-asthmatic combinations, barbiturates are also of relatively short duration of action, while therapeutic benefits have been noted with the hydroxyzine-ephedrine-theophylline combination up to 4 hours in duration.

It is believed that the non-tranquilizing pharmacologic properties of hydroxyzine help produce interdigitating effects beneficial in the treatment of asthma. Though these effects (anticholinergic, antispasmodic, antiserotonic) operate independently, they also appear to reinforce those of the ephedrine and theophylline, enhancing the value of all these drug components in the management of asthmatic patients.

Conclusion

Though measures must be taken in allergic asthma to avoid the offending allergen or to desensitize the patient, symptomatic and prophylactic drug therapy is required to alleviate bronchospasm, control secretions and edema, and

provide relief from anxiety as well as the side effects of ephedrine-theophylline. Hydroxyzine when substituted for the barbiturate in the time-honored combination containing ephedrine and theophylline appears deserving of extensive clinical trial. It is believed that this new preparation provides unusual efficacy because of the good tranquilization afforded by hydroxyzine. Equally important are the additional pharmacologic properties of hydroxyzine — antihistaminic, anticholinergic, and antiserotonic—each of which reinforces the clinical benefits of ephedrine and theophylline while offsetting some of their undesired side effects.

In a preliminary clinical trial with a hydroxyzine-theophylline-ephedrine combination (Marax) in asthmatic patients, 76% of 117 patients received excellent relief, 7% moderate improvement, and 17% no improvement.◀

Epidemic Hepatitis: Diagnostic Value of Serum Aldolase Determination

Levels of aldolase were determined in the serum of 61 children aged 16 months to 10 years with epidemic hepatitis. Of these, 38 were jaundiced, 23 not jaundiced. Aldolase values were also determined in 24 normal persons, in 33 with other noninfectious diseases, in 7 adults in contact with children with epidemic hepatitis, in 2 with measles, and in 4 with epidemic parotitis. In normal persons the average aldolase activity was 9.7 units, in those with noninfectious diseases 12.1 units, in children with measles 19.4 units, and in those with epidemic parotitis 24.5 units. In the adults contacting children with epidemic hepatitis the average was 18.3 units. In the 38 jaundiced children with hepatitis the average aldolase values were 75.4 units the first week, 46.8 units the second, 32.6 units the third, and 17 units the fourth. Average values of the 23 children with hepatitis and no jaundice were 85.3 units the first week, 41.1 units the second, 23.7 units the third, and 20.1 units the fourth.

Diagnosis of epidemic hepatitis in 5 children, with normal dysproteinemia levels and no bile pigments in the urine was made on increase of serum aldolase. Although nonspecific, increase in serum aldolase is a more reliable laboratory aid in the diagnosis of epidemic hepatitis than is the dysproteinemia test.

Leonescu, M., et al., *Ruman. M. Rev.*, 2:44-47,1958.

The Practicing Physician and the Health Officer

LEON J. TAUBENHAUS, M.D., M.P.H.,*
Brookline, Massachusetts

►*Although the attitudes of the practitioner towards the treatment of disease may differ from the methods used by the community health officer in maintaining sanitary conditions, close cooperation between the two will insure a better-protected and better-informed community as far as matters of health are concerned.*◄

Like the clinical specialist, the modern health officer is specially trained, and can, through the means at his disposal, render valuable services to physicians practicing in his community.

What is Public Health?

Public health practice differs from clinical medicine primarily in point of view and interest. Both are concerned with disease, its control and its eradication. The clinical practitioner's primary concern is the health of his patients as individuals or as families. The public health officer's concern is with the health of his patients, aggregated into a community.

This difference can best be illustrated by observing how a practicing physician and health officer look at a single disease, for example, syphilis.

Syphilis, a clinical entity due to a specific organism, usually transmitted by sexual activity, can be easily cured by proper treatment. Not given proper treatment, it can produce serious sequelae and can be transmitted to others. Both the practicing physician and the health officer have the same knowledge. At first both proceed in the same way. In establishing the diagnosis the practitioner probably uses the health department laboratory. When his patient is discharged as cured, he will have reported the disease, and may have made an effort to examine and treat family con-

*Director of Public Health, Brookline, Mass., Lecturer in Public Health Practice, Harvard University School of Public Health.

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tacts. He has, however, no power to force treatment on anyone.

The public health officer is also interested to see that the infected individual is properly treated. If adequate treatment is not available from the private physician, the health department will supply it. However, the health officer's particular interest is in finding out who else in the community is involved in the spread of this infection *to and from* the individual patient. He will make a study of the case and trace the primary and secondary contacts, their contacts, etc., and do his best to insure that all those infected are found and treated. Often the follow-up of one patient leads to the treatment of 20 or more others, many of whom will be referred to their own doctors by the public health officer.

The health officer is the person legally charged to prevent disease and to protect and promote the health of his community. Whereas the private physician can only suggest or recommend treatment, the health officer can, in cases of communicable disease, enforce treatment if its lack endangers the health of the community.

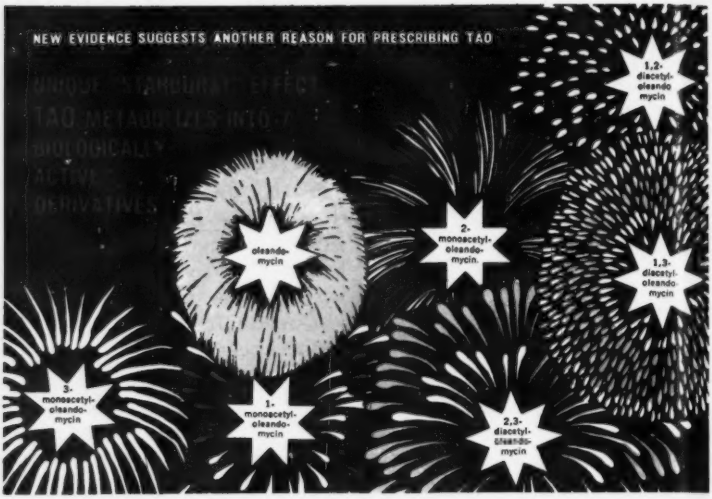
Health Officer's Work Largely Educational

Although the health officer legally has police powers to protect the public health, he rarely uses them. Utilizing many techniques, he educates and encourages his community to develop proper health practices. These include more frequent visits to the family physician. In communities where the need for certain clinical services has not been supplied by the local physicians, the health department may provide this service. Aside from certain clinical services required by local or state law, those of most health departments complement and supplement rather than duplicate those of the private physicians.

Probably the best definition of public health is that of Winslow, "the science and art of preventing disease, prolonging life, and promoting health through organized community effort." The objectives "to promote health and prevent disease" are identical with those of clinical medicine. The means ("organized community effort") are those of the speciality and not ordinarily available to doctors in private practice. Administration and community organization are as essential to the practice of the health officer as is the scalpel to the surgeon or the electrocardiograph to the internist.

The Practicing Physician and the Local Health Department

In spite of whatever free clinics a local health department con-



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1. English, A. R., and McBride, T. J.: Proc. Soc. Exper. Biol. & Med. 100:880 (Apr.) 1959. 2. Celmer, W. D.: Antibiotics Annual 1958-1959, New York, Medical Encyclopedia, Inc., 1959, p. 277. 3. English, A. R., and Fink, F. C.: Antibiotics & Chemother. 8:420 (Aug.) 1958.

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ducts, the health department increases the local physicians' private practice. Most of the clinical services offered by the health department are required by State law, or are meeting a need not currently met by physicians in practice in the locality. Generally therapeutic services, when needed, are referred to the private physician or clinic.

Disease detection services are frequently offered by health departments. Here, persons who probably do not have the given disease are screened out while those who have the disease are referred to their doctors for detailed diagnosis and treatment. The public is spared the direct cost of many normal examinations, yet those who are likely to have the disease are placed in the hands of physicians at an earlier date.

The health department collects current vital statistical data on births, morbidity, and deaths. The practicing physician, by keeping contact with the health department may keep informed on trends in reportable diseases, and so be able to make an earlier diagnosis and treat more effectively a puzzling case in his practice.

The health department also either facilitates obtaining or furnishes many vaccines, antigens, or antibiotics. At times the use of these products may be limited to certain types of cases.

Prompt laboratory testing and diagnostic studies for tuberculosis, parasitic diseases, typhoid, syphilis, and other communicable diseases are available through most health departments. In addition, the health officer himself may often be a competent consultant in cases of these types of illness.

The local health department by epidemiological studies on the diseases reported may be the means of finding and eliminating the source of an infectious or industrial disease. Its testing of water, milk, and food samples in cases of suspected contamination, and routine inspections and controls of food, milk, and water supplies prevent their becoming a source of communicable disease.

The health department can abate environmental hazards reported by the physician without involving him. It can also advise the physician on the environmental aspects of medical problems he faces, such as those produced by his own radiation equipment.

The health department furnishes advice and guidance to physicians in unusual situations such as poison control centers, civil defense emergency, airborne radioactive contamination, and other disaster situations. It may also furnish certain professional, nursing, and technical per-

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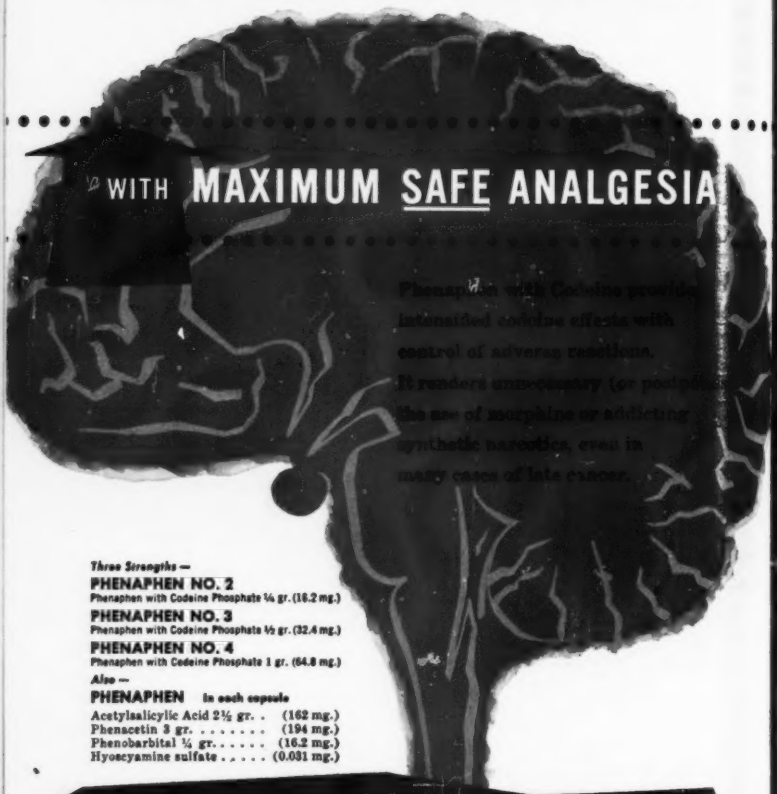

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Not every health department can always furnish all the services listed here, however, it will attempt to supply those services which its community requires.

The Physician's Obligations to the Health Department

Prompt reporting of all legally reportable disease to the local health department is a prime responsibility of the private physician. No health department can furnish morbidity and mortality information to the local doctors if that information is withheld by these same doctors. If a patient who is unhappy about an unavoidable complication of a reportable disease sues, and it is brought out that the physician did not meet his legal responsibility of reporting the case, this revelation may count seriously against him.

The physician should also report to his local health department health and sanitary hazards that come to his knowledge. His anonymity can easily be protected and the department can take proper steps.

The physician should also supply his local health department with the follow-up information on individual patients it may seek from time to time, since it will often given valuable epidemiologic information of benefit to the patient as well as the physician.

Conclusion

The public health department and the practicing physician represent two key positions of the health team. Understanding cooperation between the two will facilitate the work of each, to the great advantage of the community which they serve.◀

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REFERENCES:

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12. Phillips, F. M.: DECLOMYCIN—Seventh Interim Report. Department of Clinical Investigation, Lederle Laboratories, Pearl River, N. Y., December 4, 1959.

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SHEPARD SHAPIRO, M.D., *New York, New York*

▶*One of the most frequent side effects of antibiotic therapy is sterilization of the bowel. The resultant diarrhea produces as much discomfort as the original condition. Yogurt is beneficial in restoring the normal floral pattern of the intestine while inhibiting undesirable proteolytic organisms.*◀

Although improvements in preparations of antibiotics made in the past few years have reduced the frequency of gastrointestinal disturbances arising out of the use of these agents, such upheavals still occur and in special situations create clinical problems of considerable severity. Under certain conditions disorders of this variety interfere with the efficacy of the antimicrobial agents and, if use of the drug is prolonged, may seriously undermine the nutritional state of the patient.

Illustrative Cases

Case 1

A woman of 40 had recurring attacks of "mucous colitis" over a period of about eight years, characterized by abdominal cramps, diarrhea, anorexia, weight loss and weakness. She had been free of symptoms for two years prior to the present illness. She became ill with a pneumonic infection for which she was given terramycin, 250 mg. q.i.d. There followed gradual appearance of abdominal distress and on the fifth day of therapy bowel frequency, watery diarrhea, and recurrence of mucous colitis, which persisted for several weeks.

More disastrous may be the occurrence of similar symptoms in a patient with severe malnutrition from protracted illness. Here the impairment in nutrition induced by the acute episode may be irreversible.

Case 2

A woman of 38 with cirrhosis of the liver, portal hypertension, hypoproteinemia and ascites was receiving intensive treatment to counteract protein deficiency. An abdominal paracentesis was followed by a low-grade fever for which terramycin, 250 mg. q.i.d., was given. On the evening of the third day of this therapy there appeared frequent bowel movements, worsening on the next day to watery diarrhea which could not be controlled. The patient became comatose on the following day and died 36 hours later.

Mode of Development and Progress of Symptoms

A change in intestinal flora

TABLE 1

TETRACYCLINE CONCENTRATION (GAMMA/ML.)

No. of Patients	Hours after 250 mg. Tetracycline		
	2	3	6
1	1.025	1.210	1.350
1	.830	1.145	1.021
1	1.190	1.130	1.105
Total 3			

may be induced by antibiotics, causing hypermotility of the bowel and diarrhea which will deplete the body of essential nutritional components. To counteract this, a therapeutic supplement is needed which will obviate the digestive difficulties that have arisen but not interfere with the absorption of the antibiotic.

Yogurt Found Effective

It is believed that antibiotics also cause overgrowth of bacteria in the intestine which disturb the physiologic balance and yield products causing hypermotility and consequent nutritional depletion. Studies have demonstrated that such bacteria with pathologic implications can be inhibited by yogurt,* a preparation of pasteurized milk processed with special cultures of Lactobacillus bulgaricus and S. thermophilus.[1] Yogurt is an excellent food supplement for patients exhibiting untoward gastrointestinal patterns, including those induced by antibiotics. The results have been uniformly favorable and form the basis of this report.

Present Study

The yogurt used in this study has a custard-like consistency and is very acceptable to patients, even those in whom feeding is a problem. To determine if yogurt interferes with absorption of an antibiotic, tetracycline phosphate was administered, and followed in one hour by a half-pint of yogurt. Blood samples were obtained two, three and six hours after the antibiotic was ingested and assayed for tetracycline concentration. The results are shown in Table 1.

These results compare favorably with published therapeutically active levels.[2]

Fifteen patients were given yogurt as a dietary and therapeutic supplement after gastrointestinal

*Yogurt used in this study supplied as *Dannon Yogurt* by Dannon Milk Products, Inc., 22-11 38th Avenue, Long Island City, N.Y.

1. Seneca, H., et al., *Am. Pract. & Digest Treat.*, 1:1252-59,1950.

2. Buckinger, R. H., & Hooking, C. E., Antibiotics Annual 1954-55, Medical Encyclopedia Inc., N.Y., 1955, pp. 574-577.

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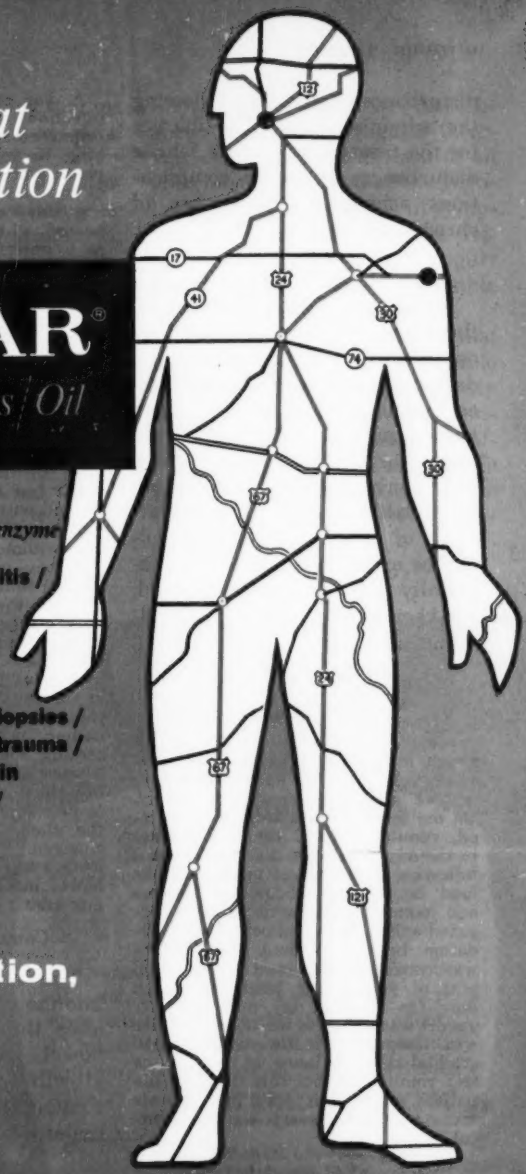

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disturbances had arisen following the administration of antibiotics for the treatment of acute febrile disturbances or acute complications arising in the course of chronic diseases.

Results

Diminution and subsidence of the digestive disorders usually occurred from within two or three days up to a week. In patients receiving antimicrobial drugs over a long period, yogurt has been helpful in lessening the symptoms of intolerance and in maintaining the nutritional state. In the treatment of active tuberculosis, tolerance to antimicrobial drugs, especially to paraminosalicylic acid, has been aided by the regular addition of yogurt to the regimen.

More Illustrative Cases

A poorly nourished woman of 72 developed bronchopneumonia for which tetracycline phosphate 250 mg. q.i.d., was given in addition to supportive and symptomatic treatment. On the third day she became nauseated, vomited several times, and later in the day developed diarrhea. On the following day she was unable to take food because of abdominal distress and became very weak. Fever persisted and signs of pulmonary consolidation became evident. Tetracycline was continued, followed by one-half pint of yogurt one hour after each dose. On the fifth day, one day after yogurt was added to the therapy, there was lessening of the diarrhea and gradual disappearance of the nausea and vomiting. From this time on, the patient was able to retain food and ate more freely. Recovery was uneventful.

A man of 68 developed pneumonic infection in an area of chronic bronchiectasis at the base of the right lung. He was given tetracycline phosphate and a codeine mixture because of troublesome cough. On the following day abdominal distention appeared, which soon became so marked as to interfere with breathing. Later in the day nausea and diarrhea developed. On the third day when he was able to take only liquids and soft foods, yogurt was given, ½ pint one hour after each dose of antibiotic, q.i.d. On the fifth day physical signs in the chest commenced to clear and temperature fell to normal. Yogurt was continued for one week longer, morning and night. By this time the patient had returned to normal activity. On two subsequent occasions slight recurrences of the disorder treated with the same regimen including yogurt resulted in prompt recovery without intestinal difficulty.

A boy of 16 was given penicillin 200,000 units orally t.i.d., in addition to local therapy, for cellulitis of the leg. On the second day of treatment he complained of abdominal distress and as the day progressed noted frequency of bowel movements and later diarrhea, accompanied by troublesome pruritis ani. (Since age 9 this patient had had irritable colon, presenting abdominal pain and diarrhea usually after indiscretion in diet.) On the third day he was given yogurt, ½ pint twice daily morning and night, the diet otherwise remaining unchanged. On the fourth day hyperperistalsis lessened and by the sixth day bowel movements were normal despite continuation of the antibiotic.

Comment and Summary

The introduction of antibiotics into the gastrointestinal tract may alter the bacterial flora of the bowel, the consequent overgrowth of the changed bacterial content from which may induce hyperperistalsis. The diarrhea re-

sulting from this, if continuing, may drain the body of essential components and thereby undermine the nutritional state. Production of vitamins within the bowel, such as that of vitamin K, may also be reduced to below the physiologic level. It is believed that the products of L. bulgaricus fermentation restore the acid producing bacteria and inhibit proteolytic organisms, thus reestablishing the pattern normally existent in the intestine.

To establish the effectiveness of yogurt, a control period would be desirable. However, it is well known that digestive disturbances persist for irregular intervals even after withdrawal of an antibiotic. It is felt that the regular and prompt cessation of symptoms of intestinal disorders following the ingestion of yogurt indicates that it was responsible for the favorable change.

These experiences indicate that the feeding of yogurt is capable of restoring to normal activity bowel function disturbed by antibiotics. When given an hour after the antibiotic, it is compatible with antibiotic plasma levels adequate for therapeusis.◀

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metabolic,
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Postsurgical Fluids and Electrolytes

PHILIP THOREK, M.D., *Chicago, Illinois*

►*Water, carbohydrates, proteins, vitamins, and the salt ions are involved in the homeostatic processes of the body to restore equilibrium following surgery. Some of the basic concepts of depletion, tonicity, and stress reaction are reviewed, and restorative technics and therapeutic solutions suggested.*◄

It is difficult in this day of "laboratory medicine" to find practical guides to the maintenance of proper fluid balance and nutrition for the postoperative patient. Numerous works have been written on this subject. However, some disagreement exists as to the type of solution and the amount of water and electrolytes necessary for the maintenance of homeostasis. Every postoperative patient must be supplied with adequate amounts of water, salt, proteins, carbohydrates and vitamins. Fats are rarely essential in the immediate postoperative care of the patient.

Water

We need sometimes to be reminded that this substance makes up about 70 per cent of the total body weight in the average normal adult, and that four-fifths of this body fluid is found in the cells, the rest in the interstitial spaces and blood vessels. In obese patients the total body water may be less than 40 per cent and therefore such individuals do not tolerate fluid imbalance well. It is important to have a simple method of determining the patient's water needs and water balance. Usually this can be determined easily and quite accurately by utilizing the rule that the average patient must be given enough water to permit him to urinate 750 to 1000 cc. per day. Numerous factors, such as excessive perspiration, diarrhea, respiratory rate, drains, fistulas and nasogastric siphonage, alter the urinary output and water needs; these require individual correction.

The daily amount of water ingested in food is some 1500 cc. An additional 5500 cc. of water or

potential water enters the esophagogastric-intestinal tract per 24 hours as: saliva 500 cc., gastric juices 1200 cc., bile 600 cc., pancreatic juice 1200 cc., and succus entericus 2000 cc. This constitutes a total of 8000 cc.—11 per cent of the body weight and over half of the extracellular water. Not all of this is present in the gastro-intestinal tract at a given time. Water absorption most likely begins in the upper small bowel and continues to and through the right half of the colon; normally, only 200 cc. is excreted in the feces. It is dangerous to state that every postoperative patient must have three quarts of fluid per day or continuous intravenous drip. The average patient will urinate 750 cc. of urine daily if 2000 cc. of water is supplied. These rules do not pertain to the nephritic or cardiac patient. If the physician wishes to determine rapidly the state of hydration of a given patient, he may test the specific gravity of the urine, or catheterize the patient and determine the amount of urine he puts out in one minute. A properly hydrated patient will void 10 drops of urine per minute. Clinical signs of dehydration should be easily detected. They are thirst, dryness of tongue, sunken eyeballs and loss of tissue turgor.

Primary Water Depletion

In primary water depletion (esophageal obstruction, coma, etc.), the extracellular fluid becomes hypertonic causing water to move from the cell to the extracellular space. Although the resulting intracellular dehydration may be marked, there may be no change in plasma volume or electrolyte concentration. Therefore, in this condition there is a small urinary output and normal or increased concentration of plasma protein, and/or electrolytes. The treatment of primary water loss consists of water replacement, best by the administration of adequate amounts of 5 per cent dextrose in water. Since only small amounts of salt have been lost, hypotonic saline or amino acid solutions containing a little sodium chloride are most desirable. The average postoperative patient requires one liter of water to replace insensible loss (breathing and sweating) plus one liter for urinary output. Four gm. (69 mEq.) of sodium chloride will usually replace the daily salt loss. Less salt and water are required the first 24 postoperative hours because of the stress response to surgery.

Sodium Chloride

Sodium chloride requirements of the average individual range between 4 and 12 gms. (69 to 208 mEq.) daily. These are altered by heat, fever, suction, vomiting, and fistulas, to mention only a

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References: **1.** Gibson, G. G.: M. Clin. North America *40*:1623, 1956. **2.** Miles, P. W.: Missouri Med. *56*:1243, 1959. **3.** Forster, H. W., Jr.: M. Clin. North America *40*: 1641, 1956. **4.** Priestly, B.S.; Medine, M. M., and Phillips, C. C.: to be published. **5.** Costner, A. N.: South. M. J. *48*:1192, 1955. **6.** Rasgorshek, R. H., and McIntire, W. C.: Am. J. Ophth. *40*:34, 1955. **7.** New and Nonofficial Drugs: J. B. Lippincott Company, 1958, p. 243.

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few conditions. "Normal saline" or "physiologic salt," a 0.9 per cent solution, is nonphysiologic; it is an isotonic solution, containing 154 mEq. of sodium per liter. The sodium content of extracellular fluid is 142 mEq. per liter. Therefore, the sodium content of an isotonic solution of sodium chloride is 12 mEq. per liter greater than the sodium content of extracellular fluid. Although this may not be an ideal relationship, it is not harmful. The chloride content of extracellular fluid is 103 mEq. per liter as compared with 154 mEq. of chloride per liter of isotonic sodium chloride. Such a discrepancy places a load upon the kidneys which must maintain a constant electrolyte balance of the extracellular fluid. These 51 mEq. of excess chlorides and 12 mEq. of excess sodium must be excreted. If the kidneys are impaired, such a load (particularly the chloride) may become serious or even lethal. Excesses of chloride may also disturb seriously the acid-base equilibrium of the body. There are 9 gm. of sodium chloride in each liter of isotonic salt solution. The administration of two or three such liters daily places 18 or 27 gms. of salt into the body. Tissue edema, dehiscence of suture line, delay of healing and/or possibly death may result. If a patient is in negative sodium balance, it may become necessary to administer more than 9 gm. It is at a time such as this that the flame photometric readings and electrolyte determinations become necessary.

Primary Salt Depletion

Primary salt depletion is more common than primary water depletion. The most common causes are vomiting, gastric suction, intestinal obstruction, diarrhea, and intestinal tract fistulas. In this condition the extracellular fluid becomes hypotonic. The kidneys attempt to combat this hypotonicity by excreting large amounts of urine and no salt. The kidneys cannot retain water in the absence of salt, therefore further water depletion also occurs even if large amounts are supplied. The plasma chloride concentration may remain normal until the kidneys can no longer excrete the extracellular water. Oliguria and anuria may precede the appearance of clinical shock. In primary salt depletion, the plasma reflects the changes in chloride or bicarbonate concentrations, depending upon which body fluid is lost.

The loss of gastric juice produces a reduction of plasma chloride (normal 100 mEq.) and an elevation of bicarbonate ion concentration (above 30 mEq.). There may also be a small drop in plasma sodium. These patients develop alkalosis. When the loss

is due to bile or pancreatic juice, there is a greater loss of sodium bicarbonate than of sodium chloride. The plasma bicarbonate is reduced below 25 mEq. and there might be slight increase in plasma chloride. These patients develop acidosis.

The treatment for primary salt loss will vary accordingly to the source of such loss. In general one may follow this plan:

1. Hypotonic salt solutions (0.45 per cent) should be used in the immediate postoperative period because of fluid and salt retention (steroid action).

2. Isotonic solutions of sodium chloride (0.9 per cent) as a general replacement should be used primarily when gastric juice is lost. Gastric juice is often hypotonic, therefore replacement of such drainage contents by the "volume for volume" rule is not always accurate. If such loss is prolonged, re-evaluation is advisable.

3. Hypertonic solutions of sodium chloride (2 to 5 per cent) are preferred in patients with pancreatic or intestinal fistulas because of the great salt loss. To attempt to compensate for such heavy salt losses with isotonic salt solutions would result in an excessive urinary output. Continuous and daily re-evaluation of these cases will determine the necessary requirements.

Potassium (K)

This cation is chiefly intracellular. The exact daily requirements are not known, however, it has been estimated that the average adult requires from two to four gm. (51 to 102 mEq.). The primary causes of K deficiency include vomiting, diarrhea, pyloric obstruction, ulcerative colitis, intestinal fistulas, prolonged administration of ACTH or cortisone, and continued usage of K-free solutions. Overproduction of ACTH endogenously may result from increased body utilization of K as occurs during the healing of burns. Clinical findings of this deficit are characterized by a triad —weakness, anorexia, and silent abdomen—which the author calls the W.A.S. triad. If cells are deprived of K, they cannot function properly—this refers particularly to muscle cells (gastro-intestinal and cardiac). Hence, we find ECG changes and distended bowel. Palpable muscles feel soft and putty-like, and if the condition continues untreated, extreme weakness, tremors and coma result. ECG findings of low voltage and flattening of the T waves are present when the K level is below 4 mEq. The plasma K may be normal or even increased in an early cellular K deficit. If alkalosis persists after adequate sodium chloride therapy and hydration, one must suspect a K deficit.

Treatment of Potassium Loss

Careful replacement is required. Since excessive K may produce a heart block and sudden death, it must be administered cautiously. It is usually contraindicated in cases of severe oliguria or anuria because of a K "pile-up." In emergency treatment from 4 to 5 gm. of KCl should be given in one liter of 5 per cent dextrose in water. After this, 3 gm. of parenteral KCl is usually necessary to maintain daily requirements. Oral administration of KCl should be instituted as early as possible (5 to 10 gm. daily) for many days, because the depletion is difficult to overcome. The reason for this is that the homeostatic mechanism of the body attempts to prevent extracellular K from going above a level of 5.5 mEq. per liter.

Protein Requirements

At bedrest, the average postoperative patient will not tear down his own proteins if we supply a minimum of 100 gm. per 24 hours. If the patient cannot take this by mouth, it must be supplied parenterally in blood, plasma, or one of the newer solutions (hydrolasates) which supply the amino acids.

Carbohydrate Requirements

Carbohydrates also should be supplied in the amount up to 100 gm. per day in the form of 5 per cent dextrose. The diabetic patient must be "covered" with insulin. Such special cases should be managed by a physician well versed in diabetes.

Vitamins

Fat-soluble vitamins A and D usually are stored in the body, but the water-soluble vitamins B and C are depleted rapidly and require replacement. Vitamin B is necessary for the proper utilization of proteins, therefore it is advisable to give from two to three ampules of vitamin B-complex per day. Vitamin C has been aptly referred to as the surgeon's vitamin, since it is essential for wound healing. The author has found it advantageous to supply 1500 mg. of cevitamic acid per day.

Some pharmaceutical houses now manufacture solutions which meet these needs. Each 1000 cc. of such solution contains 1000 cc. of water, 3 gm. of NaCl, 50 gm. of protein, and 50 gm. of carbohydrate. To these, vitamins B and C and the necessary antimicrobials can be added. Each liter of such solutions contains half of the daily requirements. It has been suggested that, following the patient's morning care, a liter of such solution be administered at the rate of one drop per second, taking three hours to give. Then the patient may be relieved of

further intravenous therapy until the evening when the second liter is given. In this way the patient receives his daily requirements of water, 6 to 9 gm. of salt, 100 gm. of protein, 100 gm. of carbohydrates, and the necessary vitamins and medicaments. Let it be stressed again that in no instance should parenteral therapy be utilized if the patient can take fluid or food by mouth.

In cases of esophageal resection, the order nothing by mouth is necessary for three days—in gastric resections for two days. Following this, the patient may have ice chips and sips of water (warm or cool). The next day tea, dilute orange juice and fat-free broth are added to the intake. By the fifth or sixth postoperative day semisolids are given and at the end of the first week, a liberal soft diet. In patients not having anastomoses, tea and water are permitted postnausea. Full liquids are given on the third day, and a regular light diet by the fifth or sixth day.

Stress reaction (Selye), affects the kidney function in such a way that sodium and water are retained and K is excreted. Therefore it is preferable to withhold some water and Na for the first 24 hours postoperatively and to supply and replenish the K loss. It has been my practice to supply in the first 24 hours 1000 cc. of water in a 5 per cent dextrose solution to which 3 gm. of KCl has been added. No NaCl is given during this first postoperative day unless there is a specific indication or depletion.◀

Macroglobulinemia of Waldenstrom

Macroglobulinemia of Waldenstrom is a chronic condition with fatal outcome occurring predominantly in older men. Symptoms are anorexia, dyspnea, loss of strength and weight, and later a tendency to general bleeding. Some patients show lessened resistance to infection, intravascular hemolysis, and general lymphadenitis and hyperglobulemia with inverted albumin-globulin index. The finding of macroglobulins on ultracentrifugation is pathognomonic. Simpler laboratory tests can make the diagnosis probable. The primary disturbance seems to be in the reticuloendothelial system.

Alvsaker, J. O., *Tidsskr. norske laegefor.*, 78: 1171-1173,1958.

YOUR PATIENTS WHO COMPLAIN OF ACHES AND PAINS WILL USUALLY BE TROUBLE-FREE FASTER

Dermatologic Use of A New Antimicrobial Medication

LEONARD D. GRAYSON, M.D., and
HILLIARD M. SHAIR, M.D., *Quincy, Illinois*

▶*Among 19 patients having bacterial infections 80 per cent showed marked improvement following topical application of the antibacterial. Fungicidal properties of this new therapeutic agent were also evident among the group of 16 with fungal conditions, where 60 per cent improvement was noted.*◀

In vitro studies have shown that 9N aminoacridine 4-hexylresorcinolate* has bactericidal or bacteriostatic effect against Mycobact. smegmatis; B. subtilis; E. coli; Staph. aureus; Staph. albus; Pseud. aeruginosa; Trich. rubrum; mentagrophytes, and gypseum; Mon. albicans; Cand. montifera; and Sacch. cerevisiae. It is also believed there is some activity against B. proteus; S. typhi; S. boydii; enterococcus; M. pyogenes aureus; H. capsulatum; M. audouini; P. pedrosi; B. dermatitides; C. neoformans; and C. immitis. It appears to be a potent trichomonicidal agent and is algaestatic. Skin sensitization tests have been reported and to date there has been no evidence of sensitization to this agent.

As shown in Table 1, 80% of bacterial infections were greatly benefited with the use of Akrinol

*Akrinol, Schering Corporation, Bloomfield, New Jersey.

TABLE 1

RESULTS OF THERAPY WITH *AKRINOL*

DISEASE	# OF PATIENTS	EXCELLENT	GOOD	FAIR	NO EFFECT	SIDE EFFECTS
Bacterial infection	19	13	3	0	3	0
Fungus infection	16	4	6	3	3	0
Eczema	7	3	1	0	3	2
Lichen planus	1	0	0	0	1	0

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TABLE 2

RESULTS OF *AKRINOL* THERAPY IN BACTERIAL INFECTIONS

DISEASE	# OF PATIENTS	EXCELLENT	GOOD	FAIR	NO EFFECT	SIDE EFFECTS
Staph. aureus	3	3	0	0	0	0
Paronychia*	3	3	0	0	0	0
Impetigo*	1	0	0	0	1	0
Hidradenitis*	1	0	0	0	1	0
Folliculitis*	6	4	1	0	1	0
Erysipelas*	1	1	0	0	0	0
Infected ulcer*	1	1	0	0	0	0
Pyoderma*	3	1	2	0	0	0

*Organism not identified

TABLE 3

RESULTS OF *AKRINOL* THERAPY IN FUNGUS INFECTIONS

DISEASE	# OF PATIENTS	EXCELLENT	GOOD	FAIR	NO EFFECT	SIDE EFFECTS
T. rubrum	5	1	2	1	1	0
T. tonsurans	1	0	1	0	0	0
T. mentagrophytes	2	0	1	1	0	0
Aspergillus	1	1	0	0	0	0
E. floccosum	1	0	1	0	0	0
M. audouini	1	0	0	0	1	0
Athlete's foot*	3	2	1	0	0	0
Tinea manuum*	1	0	0	1	0	0
Tinea corporis*	1	0	0	0	1	0

*Organism not identified

cream. In the fungus infection group 60% were improved. According to Table 2 most of the skin infections that are caused by bacteria were cured with the use of this medication. Table 3 reveals that the effect on fungus infections was variable.

The side effects consisted of a burning sensation and slight worsening of the condition. This occurred in two patients with eczema.

Forty-three patients were treated with Akrinol as a topical medication and the results tabulated. It is our feeling that it is an effective antibacterial local medication. It is somewhat beneficial in fungus infections.◀

A New Agent for the Symptomatic Relief of Myalgia of the Head

ROBERT E. RYAN, M.D., *St. Louis, Missouri*

►*It has been found that head muscle pain is due to local capillary spasm. Among 50 patients treated with this musculoskeletal relaxant 76 per cent experienced relief within 15 minutes following intravenous administration. There was no apparent change in normal reflexes, and the only side effect was drowsiness.*◄

In recent years few new agents have appeared on the drug horizon for the symptomatic relief of myalgia of the head. The pain experienced in the attack has been compared to the pain that results when a muscle is forced to exercise while under ischemic conditions.[1-3] Although the exact cause of myalgia of the head is not known, the attacks seem to be brought on by humidity change, drafts, air conditioning, changes in atmospheric pressure, fans, or any sudden increase or decrease in temperature. It may be said that myalgia of the head is a physical allergy. Since this is a form of intrinsic allergy, it is seen more frequently during seasons of wide temperature variance, i.e., spring and fall. It has been said[4] that persons with this condition have an abnormality in the vasomotor system.

During the attack either one muscle or a group of muscles is involved, the postural muscles having their origin from or insertion into, the skull bones. Any increase of tension of the postural muscles, even some forms of acute infections, may bring about an attack of this type. Myalgia of the head is due to a spasmotic contraction of the ends of the capillaries nourishing the affected area. The pain of these attacks can be relieved by dilation of these capillary structures. This has been accomplished by the use of a vasodilator such as nicotinic acid in either the oral or inject-

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2. Kellgren, J. H., *Brit. M.J.*, 1:325,1938.
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4. White, J. C., & Smithwick, R. H., *The Autonomic Nervous System, Anatomy, Physiology and Surgical Application*, Second Edition. The MacMillan Co., New York, 1941.

able form.[5] The pain in a typical case of myalgia of the head has an insidious onset, gradually increases in intensity to a peak, then subsides just as slowly, the entire process taking place in a period of a few hours.

When the pain is referred to a secondary muscle or group of muscles at some distance from the primary site, only the original circumscribed painful area is tender to touch or to pressure. Occasionally, over the points where the branches of the cranial nerves perforate the skull, secondary neurological conditions are noticed.

It has been demonstrated that wet heat and massage palliate the pain of myalgia of the head, and so finds usefulness as a supplement to the vasodilatory therapy. Peripheral blood flow can be increased by the use of an electrical apparatus such as the medcolator,[6] or a medication containing mephenesin and nicotinic acid.[7]

This paper is an evaluation of an injectable form of methocarbamol* in 50 cases of myalgia of the head. Methocarbamol [3-(o-methoxyphenoxy)-2-hydroxypropyl-1-carbamate] is derived from guaiacol glyceryl ether, an interneuronal depressant agent with definite but transient skeletal muscle relaxant properties. Pharmacodynamic studies[8] have demonstrated that methocarbamol produced a prolonged relaxing effect on skeletal muscle through a depression of spinal multisynaptic pathways with no effect on monosynaptic reflexes. The drug has shown a marked and prolonged skeletal muscle relaxing property with an apparent wide range of safety.

Method of Study

Methocarbamol in the intravenous and oral forms, was administered to a series of patients with myalgia of the head. All patients presented themselves for treatment during their attacks and all had the typical pain. The areas involved were tender to touch and the pain was of gradual onset. The stage of the attack varied from patient to patient.

The parenteral form was administered intravenously without dilution in doses of 5 cc. (0.5 gm. methocarbamol) and 10 cc. (1.0 gm.) to outpatients. When a 10 cc. dose was used, it was added to 500 cc. of normal saline solution and given intravenously at the rate of 25 to 30 drops a minute. Maintenance doses oral methocarbamol were prescribed of 1-3 gm. a day.

* *Robaxin Injectable®*, A. H. Robins Company, Inc., Richmond, Va.

5. Ryan, R. E., *Headache—Diagnosis and Treatment*, C. V. Mosby Co., St. Louis, 1954.
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TABLE 1

RESPONSE OF 50 PATIENTS TO *ROBAXIN INJECTABLE*

METHOD OF ADMINISTRATION	NUMBER OF CASES	EXCELLENT	GOOD	POOR
Intravenous Direct	25	5	12	8
Intravenous Drip	25	12	9	4
TOTALS	50	17	21	12

Results

The injections brought about prompt relaxation of the skeletal muscles in 76% of the cases, with no apparent change in the normal reflexes. In most cases, the patients began to notice relief from the myalgia attacks within 10 to 15 minutes. Many patients who received methocarbamol by intravenous drip had some relief before the administration was completed. These patients were usually required to stay in the office for an hour for this treatment. Relief of pain was greater with the intravenous drip method than when it was administered undiluted.

Rating of Response

The response to therapy was rated as follows: excellent—complete relief of symptoms within one hour; good—partial relief of symptoms; poor — no relief of symptoms. The response of 50 patients treated with Robaxin appears in Table 1.

Discussion

The symptoms of myalgia of the head sometimes come on suddenly and sometimes gradually increase in intensity to a peak and then gradually subside. The patients in this series were in all stages of the attack when intravenous methocarbamol was used to control the pain. In those patients who responded to the medication, it did not seem to matter whether the drug was given when the pain was building up or when it was decreasing. Since patients presented themselves to the physician at all stages, the effectiveness of the medication throughout the course of the attack makes it especially valuable. Most patients noticed relief from the myalgia attacks during the hour required for the administration of the medication by the intravenous drip method.

The injectable form of this preparation seems to be essentially nontoxic. In the series of 50 cases, the only noticeable side ef-

fect was a mild drowsiness in 14 of the patients (28%) which lasted no longer than an hour in any case, and was never so severe as to cause the patient to complain.

Since no side effect was reported when the medication was administered by the intravenous drip method, this method of administration might be preferable when the occurrence of mild drowsiness is considered a disadvantage.◀

Primary Ovarian Pregnancy

Positive diagnosis requires that:

1. The tube, including the fimbria ovarica, be intact and clearly separate from the ovary.

2. The gestational sac definitely occupy the normal position of the ovary.

3. The sac be connected with the uterus by the utero-ovarian ligament.

4. Ovarian tissue be present in the walls of the sac.

In 60% of cases preoperative diagnosis is ectopic pregnancy. Although 75% of ovarian pregnancies terminate in the first trimester, 25% last to the second trimester (half of these lasting to the third trimester or beyond). About 66% or the viable fetuses are stillborn, and 18.2% are malformed.

In an illustrative case, a white woman of 30 was first seen two years after having given birth to a normal living male child and three years after having had an early spontaneous incomplete abortion. A Smith-Hodge pessary had been inserted for dyspareunia six months prior to examination and was still in place. BMR was plus 8%, cholesterol 300 mg.%. Hemogram and urinalysis were normal. The pessary was not replaced. When seen again 6 weeks later, the patient stated that she felt better without the pessary. At this time she was placed on 10 mcg. liothyronine (Cytomel) daily. Basal temperature was extremely erratic, and not affected by this treatment. On microscopic examination ovarian tissue was found in the wall of the sac. At operation the sac occupied the position of the ovary and was connected to the uterus by the utero-ovarian ligament. The tube, including the fimbria ovarica, was normal, intact, and freely movable on the affected side.

Gentile, L. A., & Perrine, J. P., *New York J. Med.*, 59:4437-4439,1959.

Diagnosis and Management of Urinary Tract Infections

IAN M. THOMPSON, M.D.,* *Columbia, Missouri*

►*Anatomic and physiologic features are discussed, and diagnostic procedures useful in the successful treatment or management are outlined. Some clinical aspects of urinary infections are presented, including complications occurring in the female urinary system and some pediatric considerations.*◄

While the severity of urinary tract infection has been tempered by antibiotics and antibacterial medications, there has been no apparent lessening of the incidence of such infections. The prevalence of bacterial invasion of the urinary tract continues to insure a questioning attitude in regard to a more fruitful approach to the problem. Despite a great deal of conjecture as to the pathogenesis of urinary infections, we are still ignorant of the manner of bacterial entry in the majority of instances. The importance of structural and functional abnormalities as factors is well documented and obstruction is established as of basic etiologic significance in the majority of inflammatory processes in the urinary system.

*Chairman, Department of Urology, University of Missouri School of Medicine.

Severity Determined by Parenchymal Change

For purposes of practical management, infection in the urinary passages may be categorized as either of the upper or lower tract, irrespective of the chance of extension or intercommunication. The importance of any urinary infection is determined by the degree and extent of renal parenchymal changes. Infection in the distal segments of the system may cause disturbing symptoms, yet be of little significance, if the nephron units are not involved. Lower tract infection may lead to structural changes which can so modify the transport of urine as to cause rapid inflammatory destruction of renal tissue.

Since infection in the upper tract is of more immediate concern, inflammatory processes there constitute urgent problems. Of the two routes for bacterial invasion, the hematogenous is now less frequent than the ascending or retrograde. Hematogenous deposition of bacteria in the kidney starts a sequence of events not permissive of a casual attitude in its management. Sudden spiking fevers may give evidence of the renal etiology of the disease only when costovertebral tenderness is the more pronounced of the physical findings.

Acute Inflammation Elsewhere May Confuse

Acute inflammation of the appendix, adnexae or gall-bladder may masquerade as more likely diagnoses until the urine is carefully studied. Casual examination of the urine can be treacherous when its coccal content is unrecognized. Laparotomy has often been undertaken on the assumption that pyuria resulted from the juxtaposition of appendix and ureter. Confusion may be justifiable when physical findings point primarily to intraperitoneal inflammation and the analysis of the urinary sediment is equivocal. Occasionally one has the opportunity to utilize nitrofurantoin as a diagnostic aid, since given orally it is antibacterial only in the urinary tract. If any temporization is warranted, nitrofurantoin may differentiate processes primarily urinary from those which may, by close proximity, produce changes in the urinary sediment. However, the findings of a coccal urinary infection should cause questioning of the validity of abdominal physical findings, and reconsideration of the evidence. In most cases of hematogenous pyelonephritis the focus of infection will soon be established as renal, and urine culture and sensitivity studies will indicate the proper therapy. If a febrile course is maintained cortical abscess and perinephric inflammation must be considered. Perinephric abscess and the often obscure complications of diaphragmatic and lung involvement may result, should a coccal renal infection prove unresponsive to therapy.

Ascending Infections Easier of Diagnosis

Retrograde or ascending renal infection has generally proven to be a more easily recognizable entity owing to the frequency with which micturitional symptoms either precede or are concomitant with the febrile response. Most of these inflammations are secondary to obstruction. The source of the bacterial flora is, presumably, the colon and if the precise manner of propagation remains ob-

secure, there is abundant evidence that stasis of urine will invariably lead to infection. The propensity for stagnant urine to act as a culture medium is most evident in children who have almost insignificant amounts of urinary residuum, yet harbor infection until the impediment to free drainage has been obviated. It is equally apparent that the effects of obstruction may be compounded by such adjunctive factors as tissue necrosis, foreign body, or calculous disease.

The symptoms of urinary infection may stem from the actual source of the inflammatory process or from dysfunction of a segment of the urinary tract secondarily involved. This is particularly true of renal tuberculosis where often the only symptoms are those of vesical irritation.

Age and Sex Influence

The age and gender of a patient may suggest factors responsible for urinary infection. An elderly man with even minimal micturitional difficulty probably has prostatic hypertrophy. Any child who has fever without obvious cause should have examination of the urine for bacteria.

Approach May Be Stealthy

Most often the infections which are immediately and thoroughly investigated are those which produce prominent or severe clinical manifestations, yet the majority of infections which progress to chronic pyelonephritic renal damage are symptomatically benign and clinically unspectacular. It is for this reason that any urinary infection in which a renal component is apparent should have sufficiently complete studies to rule out important precipitating factors for such an infection. Infections which do not demonstrate clinical features connotative of renal involvement may well be treated first with an empirically selected urinary antiseptic, and if unimproved, subsequently by medications selected on the basis of culture and sensitivity studies. Should treatment with the drug of choice fail to clear the urine completely of bacteria, thorough investigation is mandatory. Seldom in the presence of an anatomic or functional abnormality in the conduit system will infection be permanently arrested by any medications; recurrence or persistence of infection is a strong indication of anatomic or physiologic abnormality.

Symptoms Only Rarely Diagnostic

Certain symptoms and signs are helpful in many instances, but for each classical colic of stone or micturitional difficulty of outlet obstruction there are many which show only symptoms of infection.

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Excretory Urography

This is a satisfactory screening process for anatomic and functional investigation of the kidneys. Prompt and well concentrated excretion of medium assures normal renal function. When anatomical delineation shows no abnormality, the source of a urinary infection will nearly always be found in the lower tract.

There should be no hesitation in the performance of retrograde pyeloureterograms in instances of hematuria or persisting infection, or whenever an excretory urogram is not entirely satisfactory. The demonstration of bacteria in renal pelvic urine in retrograde studies is the only conclusive means of determining a possible renal source of bacteria in the urine.

Routine recourse to urographic study has happily become more prevalent, yet at times to the unfortunate exclusion of basic clinical tests which may be easily performed in the practitioner's office. Examination of the wet and stained sediments of centrifuged urine requires little time and assures the existence of an infection. Post voiding catheterization is in order when bacteria are found in the urine, or in case of any micturitional difficulty. The catheter may further be useful in the performance of cystometric studies. Neurogenic disease of the bladder is a frequent precursor to infection, and the vesical symptoms may only be separable from simple irritative dysfunctions by cystometric means. An additional value of the catheter lies in the performance of cystography. The demonstration of bladder irregularities or the delineation of reflux of dye up the ureters may point to definite vesical outlet obstruction and guide therapeutic endeavor.

Urgent Symptoms Demand Special Studies

Knowledge of the specific bacterial type involved in an infection is of value only when clinical conditions are so urgent or persistent as to necessitate study of bacterial sensitivity to the various antiseptic medications. Urine cultures and sensitivities quite reasonably should be taken in instances of acute pyelonephritis or when a urinary infection has not been controlled by adequate dosage of a broad spectrum medication. (Investigation of the possible role of an obstructive factor in either instance is obviously a necessity.) Owing to increasing numbers of mutant strains of the bacteria commonly responsible for urinary tract infections, reliance must be placed almost entirely on the results of the sensitivity studies.

Clinical Differentiation of Lower and Upper Urinary Tract Infection

In many cases this rests on the prominence of micturitional symptoms in the former and the febrile response in the latter. The possibility of a silent upper tract derivation for a bladder infection must, however, be kept in mind. Cystitis is infrequent in men with no obstruction and who have had no urethritis, and should be construed as of either anatomic or neurogenic origin. In children a bladder infection should immediately suggest thorough investigation.

Special Aspects in Cases in Women

In women bladder infection is common, and despite contrary opinions, the majority are not due to use of the catheter. The shortness of the urethra, its vulnerability to coital and parturitional trauma, and its juxtaposition to the genital passages, are factors accounting for the majority of the cases of cystitis. Special care must be taken to prevent persistence or recurrence of infections. With successive courses of medication the organisms responsible for chronic pyelonephritis may become almost ineradicable. Every case of cystitis in women should at the outset be carefully investigated for possible local conditions favoring the infection. The more painstaking the examination the more frequently will local foci be found. Pelvic examinations should be carried out in women with cystitis, and vaginitis or cervicitis must be treated concomitantly with the urinary infection. A meatal stricture or stenosis may cause repeated bouts of cystitis; labial adhesions or vulvar infections may be related to recurrent urinary infections. Urinary residuum should invariably be measured, since it is evidence of anatomic or neurogenic obstruction. Correction of local factors and treatment of obstructive or neurologic deficits will curtail infection in many women with cystitis and make for more effective utilization of the urinary antiseptics.

Many women with micturitional symptoms show no infection; characteristic of these is their freedom from nocturnal difficulty. They respond most favorably to mild sedatives or tranquilizers.

The More Minute the Diagnosis the More Successful the Treatment

Proper treatment of urinary infections rests on proper diagnosis and consists of certain surgical or manipulative procedures, and employment of suitable antibacterial agents. The gradual decline in effectiveness of many of the once potent medications make it likely that no drug's usefulness will

prove permanent. Chloramphenicol has re-emerged as an effective broad spectrum medication. Resistence to sulfisoxazole has increased immeasurably in even the E. coli infections.

Two courses of action are open: an empirical selection of a medication, or a period of temporizing until the best choice can be made by use of sensitivity studies. In case of obvious acute pyelonephritis, urine culture should be made and while awaiting the results of the sensitivity studies, a drug selected on the basis of the bacteria seen in the stained smear of the urine sediment. Against cocci penicillin in dosage of millions of units is fairly effective. Erythromycin and chloramphenicol are perhaps the most suitable oral medications. Chloramphenicol requires periodic blood studies. Ristocetin and vancomycin, parenterally, may be useful in certain acute coccal inflammations. Kanamycin must be reserved for infections not responsive to safer medications. Nitrofurantoin is effective in a small percentage of coccal infections, although far more effective against bacilli.

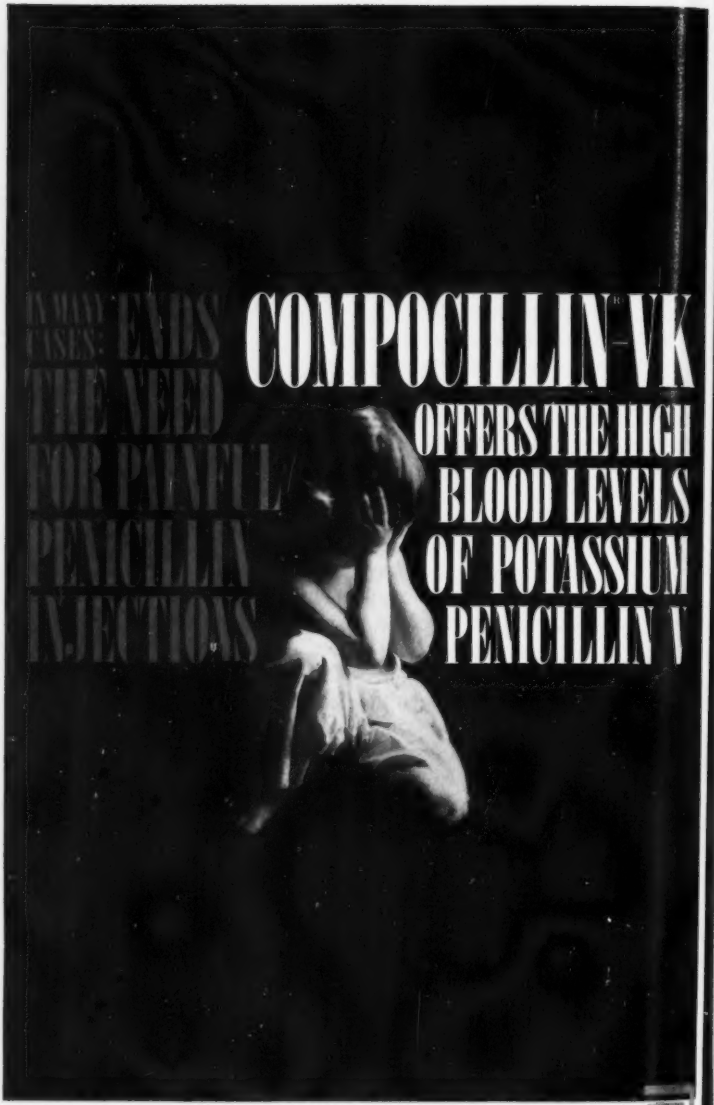
In an acute pyelonephritis, when the urine contains bacilli, and prior to the return of the sensitivity reports, either the long-acting sulfonamides or nitrofurantoin should be employed. If no beneficial response is obtained, a change to chloramphenicol would be the most appropriate. As soon as sensitivity reports are available a change to the indicated drug is made.

Increasing susceptibility of the bacilli common in urinary infections to oxytetracycline and chlortetracycline, is being shown, possibly because of their near therapeutic exclusion following promotion of the tetracyclines.

If oral routes are not feasible, and the condition desperate, parenteral preparations of chloramphenicol, oxytetracycline, the tetracyclines and nitrofurantoin should be employed.

In Chronic Pyelonephritis the Results of Therapy are Notoriously Poor

Interstitial renal infection may smolder along with or without exacerbations, and eradication of the bacteria may be impossible. Urinary bacterial content may be diminished and clinical attacks minimized or prevented by long-term courses of sulfonamides or nitrofurantoin. In the case of nitrofurantoin one cannot profitably lengthen the interval of administration although the dosage may be reduced to a maintenance level. A number of patients have been kept free of symptoms for years in this fashion. Adjunctive measures have occasionally proven helpful in the chronic infections. Trypsin, intramuscularly or orally has helped in the eradica-



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tion of chronic foci of infection. Acidification of the urine with methionine in large doses has occasionally terminated resistant infection. Mandelamine should be employed more in some resistant infections.

With no obstruction to urinary flow most bladder infections will respond to nitrofurantoin. A sulfonamide may be used initially but many of the common infections are now proving resistant to the sulfonamides. Use of antibiotics is limited by hazards of enterocolitis and blood dyscrasia. Chronic or recurring cystitis will require culture and sensitivity studies, and correction of functional or anatomical abnormalities.

Many patients discontinue medication as soon as the symptoms have been relieved. It is from such cases that the resistant bacterial flora emanate. Treatment of any infection must last at least seven days, and examination of the urinary sediment or culture studies should be carried out two to three weeks following conclusion of therapy.

Any Urinary Infection May Do Permanent Harm

All urinary infections are threats to renal function and all must be eradicated as promptly as possible. Any infection not cleared completely should have thorough anatomical and functional study of the kidneys and the conduit systems. Therapy should be continued long enough to completely destroy all the bacteria.◀

Colonic Evacuation

A new drug, bis (p-acetophenyl)-2 pyridylmethane, exerts laxation by contact with the intestinal mucosa rather than by systemic absorption or irritation with hydrostatic effect. The tablets are tasteless, stools usually are semi-formed rather than liquid, and no griping intestinal discomfort or peristaltic rushes occur. Of 70 patients, all but 3 showed satisfactory preparation of the colon with the drug. One failure occurred in a patient who had taken barium meal with a subsequent colonic stasis, while another patient had poor evacuation on the usual dose but responded well when this was repeated the following day. The present regimen for preparation of the colon, along with the usual dietary restriction, consists of 2 tablets (10 mg.) of the medication taken at 3 p.m. the day prior to examination, and a 10 mg. suppository administered at 7 a.m. the following morning.

Martin, J. A., *Virginia M. Month.*, 86:25-26, 1959.

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Treatment of Atrial Fibrillation

CHARLES FISCH, M.D., *Indianapolis, Indiana*

►*Most of these patients usually present a clinical picture of tachycardia without emergency and will respond to oral digitalis. A few require intravenous administration of digitalis because of the severity of their condition. The ventricular rate must be judiciously determined to avoid vagotonicity.*◄

The adverse effects of fibrillation are usually due to a rapid ventricular rate, control of this rate with digitalis being the initial goal of treatment. If determined at the apex, the ventricular rate is a very reliable guide to the status of digitalis therapy. However, there are two definite exceptions to this time honored "end point" of digitalization:

1. Rest alone will slow the ventricular rate.

2. Digitalis in amounts insufficient for complete digitalization will accomplish the same measureable result through its vagotonic effect.

In neither case is the patient properly digitalized despite a satisfactorily slow ventricular rate. To avoid this "vagotonic trap" the ventricular rate should be determined following brief exercise or after subcutaneous injection of 1/100 or 1/50 grains of atropine before the patient is considered properly digitalized.

There are two distinctly different clinical types encountered when treating atrial fibrillation. The first, representing the vast majority of cases, presents a moderately rapid ventricular rate (100-160 beats per minute) with or without overt congestive heart failure. Such patients are seldom critically ill and should digitalized with oral preparations of digitalis, the initial dosage being digitoxin 0.6 mg. followed by 0.4 mg. in six to eight hours. Subsequent doses of 0.2 to 0.4 mg. digitoxin are given once or twice daily (depending on the urgency of the situation) until the apical rate is about 70 beats per minute. It may be difficult, if not impossible, to achieve the optimum ventricular

rate in the presence of fever, embolization, active carditis, thyrotoxicosis, anemia and myocarditis. In such cases persistent effort to reach the desired apical rate by giving more and more digitalis will result in severe digitalis intoxication in the face of a persistently rapid ventricular rate.

Approximately 10 per cent of patients present rapid ventricular rates superimposed on severe heart disease, resulting in shock, "coronary" pain and/or progressive heart failure. Such patients require emergency care and are treated with norepinephrine and digitalis, the latter administered intravenously as lanatoside C at a dosage of 0.6 mg. every 30 to 40 minutes until the desired ventricular slowing is achieved. At that point digitalization with digitoxin is initiated, this being required because the effect of lanatoside C dissipates rapidly.◀

J. Indiana M.A., 52:1466-1467,1959.

Spinal Amyotrophy of Childhood

Spinal amyotrophy of the Werding-Hoffmann type has its onset in early life, proves fatal in from a few months to a few years, and is familial and progressive. In an illustrative case showing unusual characteristics, the patient was normal through the first year of life but showed paralysis at one year which soon became acute. At 2 years there was complete paralysis, amyotonia, and amyotrophy. The patient was able to move only the hands and feet. The facial muscles (including those involving talking and swallowing) were normal, respiration was abdominal. The parents were first cousins. Biopsy and electromyograms established diagnosis. Observation of the case extended over 12 years, during which time infections were controlled with antibiotics and sulfa drugs. Treatment of the muscular disease consisted of passive movements and stimulation of active movement. A slow but constant regression of the paralysis of certain muscles became evident between 5 and 12, frank between 12 and 14. Somatic and sexual development as well as intelligence, are normal. The patient can now sit in a chair, is able to write and to feed himself, can swim across a small pond and back unaided, and is an advanced student in high school.

Furtado, D., *Arq. pat.*, 30:522-532,1958.

Hypertension: Survey of Treatment with Chlorothiazide

CARL C. BARTELS, M.D., JAMES A. EVANS, M.D., and ROBERT G. TOWNLEY, M.D., *Boston, Massachusetts*

►*Of 65 patients undergoing treatment for hypertension, a 10 per cent drop in blood pressure was noted in 52 during studies lasting from 3 months to several years. During serum studies with 47 patients a significant lowering of potassium levels was noted, indicating the importance of serum studies during therapy.*◄

Chlorothiazide (Diuril) is a potent hypotensive agent and is one of the most widely used drugs for that purpose. The drug produces a hypotensive effect only in hypertensive patients, but its mode of action remains unknown. It has been suggested that through its diuretic action total blood volume is decreased, thereby potentiating the effect of the ganglionic blockade. In addition it has been noted that chlorothiazide is a hypotensive agent in its own right.

This survey of hypertensive patients treated with chlorothiazide is intended to:

1. Evaluate the effects of chlorothiazide as a hypotensive agent.

2. Compare its effects with and without the simultaneous use of ganglionic blocking agents or previous splanchnicectomy.

3. Determine its effect on potassium excretion as measured by serum potassium levels and electrocardiographic changes.

4. Determine the indications for and contraindications to its use in the treatment of hypertensive patients.

Method of Study

A series of 65 patients having hypertension without edema was the basis for study. Of these patients, 21 had grade 3 or 4 hypertension as determined by the Keith - Wagener - Barker method for the classification of ocular fundal changes. In 23 patients, ganglion blocking agents had been given prior to and during initia-

tion of chlorothiazide therapy, while in seven splanchnicectomy had been performed previously. All patients started on chlorothiazide therapy had had follow-up studies for at least three months to as long as several years. In most cases chlorothiazide was given twice daily—1.0 Gm. being the maximum and 0.25 Gm. the minimum daily dosage—while therapy with previously given hypotensive drugs was continued.

Basal blood pressures were determined by averaging those obtained prior to treatment with those averaged over the ensuing period of treatment with chlorothiazide (from two to seven months). Serum potassium determinations were obtained twice a week for the first two weeks and then twice a month or at monthly intervals thereafter. All patients were given a sodium-restricted diet during the study, and serum sodium levels were determined in 47 patients.

Results

A decrease in the mean blood pressure of over 10 per cent was noted in 52 (80 per cent) of the patients. Only two of the 21 patients with grades 3 and 4 hypertension showed less than a 10 per cent drop in the mean blood pressure. Of the 23 patients receiving ganglionic blocking agents, three failed to show a significant drop in blood pressure. All of the seven patients having undergone splanchnicectomy showed a pronounced drop in blood pressure, the average drop being 52/39 mm. Hg (27 per cent in the mean blood pressure). Ganglionic blocking agents given two of the patients having undergone splanchnicectomy could be discontinued when chlorothiazide was administered. Of the 23 patients given ganglionic blocking agents, this therapy was discontinued in 12 when chlorothiazide was administered, while in an additional 6 the dosage could be reduced by one-half to two-thirds. Although a drop in blood pressure was noted during chlorothiazide therapy in 77 per cent of the patients with grades 1 and 2 hypertension, this was usually less than that demonstrated in the patients with grades 3 and 4 hypertension.

A striking finding was that 28 (43 per cent) of the patients showed a drop in serum potassium levels to 3.5 mEq. per liter or below. Of these 28, the average fall was 1.5 mEq. per liter, despite the fact that 12 had received 2 or 3 Gm. of potassium chloride daily from the time chlorothiazide therapy was started. Although the fall in serum potassium levels was usually first apparent seven days after institution of chlorothiazide therapy, in one patient

a drop from 4.5 mEq. to 3.3 mEq. per liter was noted after the fourth day.

Comment

This series indicates that chlorothiazide is an effective agent in the treatment of hypertension. In grades 3 and 4 hypertension it augments blood pressure response to other hypotensive agents so that fewer and less frequent doses of the latter are needed. In orally administered doses of 500 mg. daily, chlorothiazide can produce a significant serum potassium level reduction in patients with or without normal renal function. For this reason it appears necessary to periodically determine serum potassium levels in patients receiving this agent for hypertension on a long-term basis. Such patients should be instructed to interrupt use of chlorothiazide when conditions associated with diarrhea and vomiting occur, since these could produce additional potassium losses resulting in severe potassium depletion.◀

J.A.M.A., 170:1796-1802,1959.

Thyroid Hyperfunction Syndromes

A series of 20 hyperthyroid patients (17 women and 3 men) aged 50 to 70 complained of repeated attacks of cardiac decompensation, periods of nervous depression, and loss of weight during the past few months. All 20 had tachycardia and tremor, 5 atrial fibrillation. Hyperthyroidism was of either the apathetic or the exophthalmic type. Goiter and exophthalmos were either mild or nonexistent in the apathetic type, the constant psychic feature in these cases being depression. In 7 menopausal women the symptoms of exophthalmic type hyperthyroidism were the same as those in younger women, the constant psychic feature being nervous tension. All patients initially received methylthiouracil for several days in 3 or 4 daily divided doses totalling 0.15 to 0.3 gm. Maintenance dosage was individually determined for 3 or 4 months until complete remission was obtained in all cases. Remission lasted for several years after discontinuation of treatment in all but 2 patients. Of these 2, one had a recurrence 7 months and the other 1 year after the first remission. Second remission, also achieved by administration of methylthiouracil, has lasted for several months.

Quevedo, C. de N., & Rovira, M. S., *Med. Clin.*, 31:83-105,1958.

Cause of Polio in Triply Vaccinated Individuals

JONAS E. SALK, M.D., *Pittsburgh, Pennsylvania*

►*Varying potencies of commercially prepared vaccines appears to be the underlying factor in the occurrence of poliomyelitis in triply vaccinated children. Solution of the problem appears to be the use of the smallest number of doses of an optimally effective vaccine, rather than multiple inoculations with weak vaccines.*◄

In five seasons of observing the pattern of poliomyelitis in vaccinated and unvaccinated individuals, the question arises as to why some having received three doses of the vaccine still contract the disease. Possible explanations include:

1. Certain batches of vaccine may be of less than optimal potency.

2. Some persons may be unusually unresponsive, even though the vaccine is of optimal potency.

3. The immunologic response may have dissipated rapidly.

4. The poliomyelitis virus may have reached the central nervous system by a route other than the bloodstream, thereby bypassing the influence of the serum antibody.

5. The causative viral agent may be different from that specifically protected against by the vaccine.

Findings in Children

In 4,617 children having received three injections of commercially or laboratory prepared vaccine it was shown that, generally, the larger the dose the greater the virus-neutralizing capacity found in the serum. It was also observed that antibody titers were considerably higher in the children receiving the laboratory prepared vaccine than in those receiving comparable doses of the commercially prepared vaccines. Antibody levels in these children remained constant one to two years following third inoculation. Similar variations were observed in 2,709 children having received

three injections of three differently prepared vaccines.

Antibody Response to a Fourth Dose

For the group of 4,167 children, 462 showing little or no detectable antibody formation were given a fourth dose of laboratory-prepared vaccine. Additional paired serum samples were available from 63 children given a fourth dose of a commercially prepared vaccine by their own physicians.

Results in the 462 children showed a marked increase in antibody concentrations, in most instances comparable to the levels induced by a third dose when prior inoculations were made with vaccines of good potency. The group of 63 children given the fourth dose with a commercially prepared vaccine also showed marked increases in antibody levels.

Stool specimens in 103 triply vaccinated patients collected within 14 days of onset of illness showed: Polio-viruses in 55 (type 3 in 39, type 1 in 15, and types 1 and 3 in 1); Coxsackie A9 in 3, B3 in 1, B4 in 2, and B5 in 7; and ECHO-9 in 7. The remaining 28 specimens as yet have failed to reveal viruses, and are still being studied. Of the illnesses suggesting paralytic poliomyelitis and from which virus was isolated, one-fourth were due to Coxsackie or ECHO organisms.

Control of Vaccine Potency

The foregoing observations point to vaccine potency as the critical variant in immunologic effectiveness. The role of unusually unresponsive persons cannot be evaluated fully until optimally effective vaccines are more readily available. From the present data, however, it appears that such individuals are rare.

Solution of the problem appears to be not one of multiple inoculations with weak vaccines, but rather the use of the smallest number of doses of an optimally effective vaccine. Potency testing procedures are currently undergoing revision to make vaccines of this type generally available.◀

J.A.M.A., 169:1829-1838,1959.

Acute Pancreatitis in 100 Patients

A. V. POLLOCK, M.B., F.R.C.S., *Leeds, England*

►*The results of a study among 100 patients having pancreatitis revealed that differential diagnosis must eliminate other abdominal disorders: only half presented all the classics symptoms. Catabolism must be retarded without resorting to surgery, for recurrent attacks are rare among survivors.*◄

Of 100 patients (71 female) with acute pancreatitis, half the men and three-quarters of the women had abnormal gall-bladders, in most cases cholecystitis with stones. Only six patients showed evidence of stones impacted at the lower end of the common bile duct. In no patient was the disease associated with alcoholic excess. Constant time relation between the ingestion of food and the onset of an attack of acute pancreatitis was not observed. In a number of patients, pre-existing intolerance to certain foods (notably fats) was found.

Apart from two patients with pancreatitis induced by transduodenal sphincterotomy and pancreatography, there was only one case of postoperative pancreatitis, one each of traumatic rupture of the pancreas and acute pancreatitis, and two of pancreatitic carcinoma. Five patients died soon after admission, of whom four were comatose and one was anuric on admission. All the remaining 95 patients had abdominal pain classifiable as one of three types: Sudden onset of pain radiating to the back (61), sudden onset of pain not radiating to the back (18), gradual onset of pain with or without radiation (16). The pain was epigastric, right or left hypochondrial or lower abdominal, usually sharp and severe, occasionally colicky, and usually responded fairly quickly to bed rest and analgesics unless a pseudopancreatic cyst formed, in which case the pain might be unrelenting and severe.

Classically, an attack of acute pancreatitis is a sudden onset of severe constant abdominal pain radiating through to the back, and frequently accompanied by vomiting. The vomitus contains bile, but

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only rarely small-intestinal contents. The classical symptoms of acute pancreatitis—pallor, sweating, cyanosis, low blood pressure, oliguria, and abdominal tenderness and rigidity—were present in half the patients. Shock due to fluid loss sometimes dominated the picture and suggested myocardial infarction.

The most common erroneous provisional diagnosis was perforated peptic ulcer in 29 patients. Of these, 16 were operated on. In the remaining patients differential diagnosis had to be made between cholecystitis, appendicitis, and pancreatitis. Of the 100 undoubted cases of pancreatitis, nine were incorrectly diagnosed until necropsy and 35 until laparotomy, the remaining 56 being correctly diagnosed by the clinical picture and estimation of the serum amylase. Thirty-two patients developed clinical or latent jaundice, while only five showed serum bilirubin levels within normal limits. Three patients were known to be diabetic before the onset of their attack. Fourteen had high fasting blood sugars or diabetic glucose-tolerance tests during or after their attacks of pancreatitis. Of 36 patients in whom the serum calcium was estimated during the attack of pancreatitis, the level was normal (between 8.5 and 11 mg. per 100 ml.) in 30 (four of whom died), and between 5.6 and 8.2 mg. per 100 ml. in six, all of whom developed clinical tetany and died despite massive intravenous administration of calcium gluconate.

Disturbances of fluid and electrolyte balance and extrarenal uremia in 17 patients proved fatal in 12. In these patients acidosis was as common as alkalosis. Response to treatment was poor. Two patients with hypoproteinemia and two of the three with hematemesis or melena also died. Of 12 developing a palpable mass during their illness, this was epigastric in 10, in the right iliac fossa in one, and in both situations in one. In two the pancreatitis was secondary to carcinoma of the pancreas, no direct attack on the mass being made, while in two others it resolved spontaneously. The remaining pseudo-cysts were drained, five into the stomach and four to the exterior. One patient in each of these two groups died —the patient with gastrocystostomy during operation and the other of prolonged loss of pancreatic juices. The other seven patients recovered.

In all, 26 patients died. Mortality seemed to depend more on the severity of the attack and the resistance of the patient than on the treatment employed. Severity of attack (apart from lowered serum calcium), development of diabetes, and the significance of

uremia and hypoproteinemia, is difficult to prognosticate in the individual patient. The level of amylase activity in the blood does not reflect the outlook, but a prolongation of the elevation indicates continued activity of the disease and carries a higher mortality rate.

Provided no heroic surgery is undertaken, immediate operation has no deleterious effect on survival. Of 30 patients in this series operated on during the first week of their illness, six (20%) died. Five of these were moribund and died within 24 hours. Of the 65 patients deliberately treated conservatively, 15 (23%) died. Many patients recovered from an attack of acute pancreatitis completely and have had no further trouble, or only mild indigestion, during the one to five years that they have been followed. Twenty-five gave a history of previous similar attacks, in five of whom a diagnosis of acute pancreatitis was confirmed at laparotomy. Of the 74 surviving patients, 13 (17%) have had subsequent similar attacks, in six of whom the diagnosis was confirmed at laparotomy or by gross elevation of the serum amylase level. Of the 11 having had at least two proved attacks of pancreatitis, two died in their second attack, one recovered from the second attack, four are in good health from one to four years after their second attack, and four have had transduodenal sphincterotomy, one of whom died and three of whom showed satisfactory results up to 18 months.

The basic principles of management of patients with acute pancreatitis are resuscitation, control of superadded infection by administration of antibiotics, and control of metabolic and electroylte disturbances. There is considerable dispute about other aspects of treatment, such as antispasmodics, antitryptic substances, corticoids, and operation. Fifteen patients in this series had immediate intravenous infusions of one to three liters of blood or plasma, and a further 11 intravenous infusion of electrolyte solutions. Of these 26 seriously ill patients 13 died, but only three within five days of the onset of their illness. In 70 of the patients treated with penicillin or other antibiotics, results were on the whole disappointing. Septic complications were fewer, but many died of uncontrollable metabolic and electrolyte disturbances.

The main problem with severe cases has been their catastrophic catabolism, and weight loss (up to a kilogram a day), impossible to control. In a few who have survived, no particular treatment appeared to mark a turning point. Results of blood transfusions, high-protein forced feeding, and

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PARAFON†
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corticoids have been disappointing.

Atropine and other drugs with similar action were used in 12 patients without noticeable effect on the course of their illness. Most patients who needed analgesics were treated with pethidine.

It is generally accepted that immediate operation in patients with pancreatitis can do no good, and that elective surgery should await the subsidence of the acute attack. On the other hand, diagnostic laparotomy has not been harmful. In any case it is preferable to establish diagnosis by laparotomy than to miss another condition with an elevated serum amylase level mimicking it.

When a mass becomes palpable there may be a temptation to explore it with a view to drainage. This should be resisted for two reasons: First, some masses resolve spontaneously, and second, external drainage of a recent pseudo-pancreatic cyst invites the occurrence of a pancreatic fistula accompanied by loss of electrolytes and protein. Transgastric anastomosis of the anterior cyst wall to the posterior stomach wall has proved effective in five patients recently. Barium-meal x-ray studies have shown no trace of the cysto-gastrostomy in these patients after as short a period as one week. Apparently the cyst, having discharged into the stomach, does not fill up again with gastric contents following this procedure.

After an attack of pancreatitis, the traditional view is that the gallbladder should be removed and the common duct explored if it is dilated. There is some evidence that after cholecystectomy (or if the gallbladder is not functioning), the pressure in the common duct may exceed that in the pancreatic duct, resulting in bile reflux and recurrent attacks of pancreatitis. In the present series cholecystectomy has not been found to protect the patient against attacks of pancreatitis, these patients having had recurrent attacks of pancreatitis following this procedure.

The majority of patients recovering from an attack of pancreatitis suffer few after-effects, and recurrent pancreatitis is a rare disease.◀

Brit. M.J., 1:6-14,1959.

Clinical Trial of Guanethidine Sulfate in Hypertension

EDWARD D. FROHLICH, M.D., and
EDWARD D. FREIS, M.D., *Washington, D.C.*

▶*Clinical trial in 15 patients indicates that guanidine sulfate provides an action similar to that of ganglionic blocking agents without inhibiting parasympathetic activity. Treatment with this agent should be restricted the more severe and resistant cases not amenable to standard therapy.*◀

Effects noted in 15 hypertensive patients are consistent with results in pharmacologic studies suggesting that the antihypertensive action of this drug is attributable to inhibition of efferent sympathetic nerve activity at some peripheral site. Following a control period of two weeks when all antihypertensive drugs were withdrawn, therapy was initiated on a schedule of 50 mg. orally each morning, the dosage being increased or decreased according to response, and continued for periods varying from four to nine weeks (mean, six weeks).

Determination of Dosage

Effective daily dosage varied from 12.5 to 150 mg. (average, 50 mg.). Antihypertensive activity of a given effective dosage was usually not apparent for the first 24 hours of therapy, and often progressed over the following two or three days. Persistence of action for as long as a week was noted after discontinuation of therapy. This cumulative effect could precipitate severe orthostatic hypotension and other side effects associated with overdosage if dosage were raised too rapidly. No evidence of tolerance or resistance to the antihypertensive effect was noted.

Antihypertensive Effect

The response to guanidine sulfate was characterized by a potent, orthostatic, antihypertensive effect similar to that seen with the ganglionic blocking drugs but

without the side effects of parasympathetic blockade. Reduction of systolic and diastolic pressures averaged 7/4 per cent in the supine, 18/14 per cent in the sitting, and 27/26 per cent in the erect position.

Side Effects

Heart rate with the patient supine was decreased to an average level of 57 beats per minute (range, 44 to 68). Although reflex increase in heart rate was not blocked, average increases were to 65 in the sitting position, to 71 in the erect. Other side effects suggesting parasympathetic stimulation (or parasympathetic action unopposed by sympathetic activity) included nasal stuffiness in three patients, drooping of the upper eyelids in two, and diarrhea in five. The diarrhea, even though severe in some, was readily controlled by methantheline bromide (Banthine). Impotence was a complaint in four cases, this different from that seen with ganglionic blocking agents and similar to that caused by lumbar sympathectomy (i.e., inhibition of ejaculation but retention of libido and capacity for erection. With excessive dosage, orthostatic faintness and weakness were usual, and syncope was seen in one case. Mild intermittent blurring of vision, without disturbance in pupillary accommodation, was reported in several cases but disappeared as treatment was continued. There were no significant changes in the hemogram or the blood urea nitrogen level.

Recommendations

Preliminary study suggests that two measures may be helpful in achieving optimal therapeutic action with minimal side effects:

1. Begin guanidine sulfate therapy with 12.5 mg. once daily for the first week, increasing this with increments of 12.5 mg. at weekly intervals.

2. Have the patient keep a daily record of blood pressure in the erect position, instructing him to discontinue medication if the pressure falls below a specified level.

Administration of chlorothiazide may be helpful as an adjunct to prevent wide diurnal swings of blood pressure. Guanidine sulfate should probably be restricted to the more severe and resistant cases not satisfactorily controlled by chlorothiazide alone or with hydralazine or reserpine.◀

M. Ann. Dist. of Columbia, 27:419-422,1959.

Observations on the Relationship of Warts and Carcinoma

JAMES R. HOON, M.D., *Sheboygan, Wisconsin*

►*The viral origin of warts has been noted during histological investigations and a similarity to cancer has been noted. Of 75 cases studied, only 1 showed coincidence of warts and carcinoma, suggesting that an establishment of an immunologic relationship might result in effective prophylactic therapy of cancer.*◄

Verrucae vulgaris (warts) are considered to be of viral etiology since they are transmissable both through implantation of wart fragments and through cell-free filtrates, and since virus-like particles have been noted in electronic microscope and histochemical studies. Although they do not become malignant despite exposure to a number of carcinogenic agents (proprietary wart remedies, radium and x-ray therapy, surgical excision and electrodessication), many reported observations indicate extraordinary relationships between a variety of verrucae and carcinoma. Clinically, monitory verrucous dermatoses have been described in association with visceral cancer, while experimental observations suggest that the virus of the verrucae vulgaris may on occasion hasten malignant degeneration of benzopyrene warts on rabbits' ears. It has been questioned whether or not verrucae vulgaris merit inclusion under the classification "neoplasm" since they disappear spontaneously.

These observations emphasize the desirability of immunologic studies of warts, both in relation to themselves and to their association with malignant changes in the host.

Present Study

A total of 75 patients with carcinoma of the colon, breast, thyroid, uterus, cervix, and skin, and abdominal Hodgkin's disease, were examined over a period of two years. Of these, only one pre-

sented warts at examination. Considering the immunologic possibilities involved, two cases in this series are of particular interest:

CASE 1

A female of 61 had warts during childhood but none subsequently. In 1944 she had developed a small carcinoma of the cervix, confirmed by biopsy and treated with radium. On repeated examination since that date no recurrence was observed. In 1955 this patient developed a verruca vulgaris of the hand, removed by elecrodessication.

CASE 2

Another female patient, aged 60, stated that a number of persons in her family had warts during childhood, but that she had had none. In 1953 this patient underwent right radical mastectomy for scirrhous carcinoma. Examinations every six months since that time revealed no recurrence until 1958, when a nodule removed from the abdominal wall in the left lower quadrant of the abdomen revealed metastatic carcinoma similar to that removed from the right breast. At this examination the patient presented a small, pale, fresh-appearing verruca vulgaris of the web area of the palm between the thumb and index finger measuring about 2.5 mm. in diameter. Biopsy of this lesion established the diagnosis of verucca. According to the patient it was not noticed previously and could not have been present for more than two or three weeks. This patient represents the only one in this series showing evidence of a verruca vulgaris coexistent with a malignant growth.

Conclusions

Although the evidence presented is insufficient to establish that an immunologic antagonism exists between verrucae vulgaris and malignant growth, it is sufficiently suggestive to stimulate further investigation of this relationship. If such an association becomes established, a reliable test for cancer as well as an important aid in its prevention may be developed.◀

Wisconsin M.J., 58:467-469,1959.

Common Cold: Treatment with Citrus Bioflavonoid

Of 176 cases of common cold treated with an oral preparation containing 100 mg. ascorbic acid and 100 mg. citrus bioflavonoid complex (C.V.P.), 160 showed almost immediate clinical response.

Dosage was one capsule 4 times daily. The majority of cases without bacterial complication showed complete abatement of symptoms within 72 hours (usually within 24 hours). Prophylactic administration of this preparation at a dosage of 2 capsules daily for periods of up to 2 years also produced a sharp decrease in common colds among 62 patients with a history of high susceptibility. During the course of this preventive therapy 22 of these 62 patients experienced no colds or attacks of influenza, while the remainder experienced only one mild episode of "cold."

Sobel, I. J., *J.M.S. New Jersey*, 56:625,1959.

Facial Actinomycosis Misdiagnosed as Tetanus

JAMES GRAHAM, M.D., F.A.C.S., *Auburn, Illinois,*
KENNETH MALMBERG, M.D., ROBERT PATEY, M.D.,
and ALAN RUBENSTEIN, M.D., *Springfield, Illinois*

►*The clinical symptoms and signs resembled tetanus, but after one year's observation, the diagnosis of actinomycosis was substituted. The possibility of actinomycosis should be kept in mind in obscure conditions around the cervical-facial area, particularly where a mass or infiltration is palpable.*◄

Trismus has been observed frequently as a feature of actinomycosis when the disease occurs in or in proximity to the mandible.[1,2] This brief report deals with a case in which the trismus was so marked following a crushing injury to a finger that a diagnosis of tetanus was made.

Case Report

A man of 33 years was referred from his family physician to the surgical service of the Springfield Clinic because for two weeks he had difficulty in opening his mouth. The jaw muscles stiffened gradually until he was barely able to open his mouth. Four and one-half weeks previously the patient had "mashed" his left index finger on a grinding wheel, for which he had been treated and given a "tetanus shot." About two weeks after the injury soreness in the mid-lumbar area of the back was felt when getting out of bed. This lasted about a week.

When examined, his canine teeth could not be opened more than three-eighths of an inch. There was tenderness over the left masseter muscle. The left index finger was swollen, red, and tender in the distal portion, similar to a complete paronychia. There was a subungual hematoma, and an old laceration along the medial side of the nail. X-ray examination of the mandible was normal.

The patient was hospitalized the following day at which time the finger nail of the left index finger was removed, and the area debrided. Cultures taken from this area were negative for Clostridium tetani. Blood count, urinalysis, NPN, and blood sugar during hospitalization were normal. The patient was given 100,000 units of tetanus antitoxin and 1,200,000 units penicillin daily. The next day he was much improved, and was discharged five days later with much

1. Choukas, N. C., *Oral Surg.*, 11:14-19,1958.
2. Hertz, J., *J. Internat. Coll. Surgeons*, 28: 539-555,1957.

more motion of his jaw. He was afebrile during the hospital course.

Ten months later, the patient's jaw again became tight. Examination at this time revealed a localized enlargement palpable on the anterior, inner aspect of the left masseter muscle. This lesion was not tender. The patient was treated with ACTH and skeletal muscle relaxants for four weeks without improvement. The mass varied in size from time to time and could not always be felt. Dental consultation failed to confirm malocclusion, considered a possible diagnosis.

Because the patient failed to improve and because his canine teeth could not be separated more than one-half inch, he was again hospitalized. The palpable mass was explored through an external approach. When the masseter muscle was reached, it was split in the direction of its fibers about three-eighths of an inch posterior to its anterior border. The mass was palpable beneath the heavy medial fascia of the masseter muscle. This fascial layer was split in a vertical direction and a large encapsulated area of necrotic debris was encountered. This material was removed by currette. In the debris a three millimeter hard yellow mass resembling a sulfur granule was noted. Mycostatin powder was instilled into the area, which was drained.

The pathologic report confirmed the suspicion of actinomycosis, as did culture of the material. Microscopic report is as follows: "Microscopic examination of the curettings reveals dense granulation tissue. Granulation tissue consists of heavy infiltrations with plasma cells, lymphocytes, and large numbers of macrophages filled with lipoid characteristic of foam cells. Superficial portions of the granulation tissue are infiltrated with polyps. The nodule submitted separately consists of several large sulfur granules consisting of masses of mycelial fragments surrounded by neutrophilic exudate. The findings are quite typical of an actinomycotic abscess."

The patient was treated in the hospital with Mycostatin 1,000 units daily, Chloramphenicol 1,000 mg. daily, 1,200,000 units daily of penicillin as well as saturated solution potassium iodide. The patient had four days of morbidity postoperatively, with temperature as high as 102.4° F. orally; then the temperature became flat and the course uneventful. The incision healed promptly without any subsequent drainage.

The patient was discharged from the hospital after one week and continued daily penicillin injections (1,200,000 units daily) for four months. He has had no evidence of recurrent actinomycotic activity to date (10 months after operation).

Discussion

The interesting feature of this case is its resemblance, due to coincidental features, to tetanus. In retrospect, we can say this was not the typical appearance of tetanus; but when faced with the combination of a crushing, infected wound of the finger associated with trismus, and no other apparent cause for trismus, tetanus is naturally considered as a probable diagnosis. It is also interesting that the actinomycotic lesion was masked by vigorous antibiotic therapy during the initial hospitalization, a point noted by other authors.[3] The duration and the degree of disability suffered by this patient, coupled with the relatively small size of the lesion which made its diagnosis difficult, reemphasize the need for keeping actinomycosis in mind in obscure conditions around the cervical-facial area.

3. Herberts, G., & Sandstrom, J., *Acta otolar.*, 48:458-464,1957.

Actinomycosis appears to be increasing in frequency. Excellent reviews of cervical-facial actinomycosis have been written recently.[1-6] Practically all the antibiotics have been used in the treatment of actinomycosis, usually with a high proportion of cases responding. Penicillin, chloramphenicol,[7] oxytetracycline,[8] tetracycline,[9] chlortetracycline,[10] the sulfonamides, and recently isoniazid[11,12] have been successfully employed in treatment. The most widely used and apparently most universally effective drug in the treatment of this disease is penicillin, which should be used in massive doses for a long period, certainly for several weeks after apparent arrest of the disease. This is combined with surgical excision of infected tissue, drainage where indicated, and removal of diseased teeth if any are involved. The Johns Hopkins Hospital group[13] advocates a combination of initial massive penicillin therapy, wide surgical excision of infected tissue, and long continued penicillin therapy in a dosage of 2 to 5 million units per day for 12 to 18 months after excision.◄

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7. Littman, M. L., Phillips, G. E., & Fusillo, M. H., *Am. J. Clin. Path.*, 20:1076-1078, 1950.
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13. Harvey, J. C., Cantrall, J. R., & Fisher, A. M., *Ann. Int. Med.*, 46:868-885,1957. *Illinois M.J.*, 115:271-273,1959.

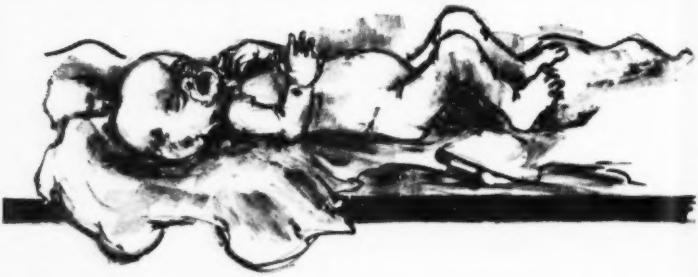
Strangulated Obturator Hernia

Pain in the inner surface of the radix of the thigh, swelling of the thigh on examination by rectum or vagina or marked sensitiveness of Scarpa's triangle are important in the diagnosis of strangulated obturator hernia. This type of hernia should be considered especially in cases of intestinal occlusion. Treatment is intervention through the abdomen, followed by femoral incision if this is insufficient. When the diagnosis of this strangulated hernia is made or the condition strongly suspected, a median subumbilical laparotomy, with the patient is an exaggerated Trendelenburg position, affords a clear view of the operative area.

Muraro, U., *Riforma med.*, 73:332-336,1959.

VERSATILE FURACIN

effective by intrapleural instillation[1]



the situation: Four-month-old infant with staphylococcal pneumonia and empyema resistant to most antibiotics was allergic to antibiotic chosen after sensitivity tests. Thoracentesis produced 30-40 cc. of creamy, purulent fluid. Organism was Staphylococcus aureus, coagulase positive.

then Furacin was instilled: 0.2% Solution was diluted equally with physiologic saline and 10 cc. of mixture instilled twice daily into pleural space, with suction catheter clamped off for 1 hour. Fluid almost immediately became thinner and less viscous. Twenty-four hours later infant was less irritable, voluntarily started taking food. Instillations stopped. FURADANTIN® Oral Suspension prescribed. Recovery uneventful.

1. Perkins, J. L.: Kansas State M. J. (to be published).

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FURACIN has been in clinical use for more than 13 years. Today it is the most widely prescribed single topical antibacterial agent. Like other nitrofurans, FURACIN remains effective, even in pus, sera or exudates, against pathogens which have developed—or are prone to develop—resistance to antibiotics.

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EATON LABORATORIES, NORWICH, NEW YORK

Kaposi's Disease

J. W. WELCH, M.D., V. E. CHESKY, M.D., and C. A. HELLWIG, M.D., *Halstead, Kansas**

►*An interesting case of Kaposi's disease is reviewed briefly from the standpoint of history, incidence, etiology, diagnostic features, pathology, treatment problems and prognosis. Any measure for control of the disease is dependent upon early accurate diagnosis and correct initial therapy.*◄

Kaposi[1] in 1872 first described a disease now generally known as Kaposi's sarcoma which he named "idiopathic multiple pigmented sarcoma." In 1894 Kaposi[2] altered the name of the disease to "idiopathic multiple hemorrhagic sarcoma." Since that time many investigators have assayed to change the name to correspond to their views as to the origin of the disease process. As a consequence many names are extant in the medical literature, but the eponym has persisted and the disease is commonly known as "Kaposi's sarcoma" or "Kaposi's disease."

*From the Hertzler Research Foundation, and the Hertzler Clinic, Halstead, Kansas.

1. Kaposi, M., *Arch. Derm. Syph., Berlin*, 4: 265-273,1872.
2. Kaposi, M., Urban und Schwarzenberg, Berlin, 1899.

Incidence

The medical literature contains over 700 reported cases, many of them isolated case reports. The justification for adding yet another case report to the existing literature is primarily because the case to be presented is an interesting one, and secondarily, to call attention to the fact that the lesion, while not uncommon, may be easily overlooked or misdiagnosed and overtreated or undertreated at various stages of its progress, with painful results. Case reports appearing in the literature at intervals of two to three years should serve to keep physicians aware of the disease, thereby facilitating early accurate diagnosis.

Kaposi's sarcoma is probably more common than the statistics indicate, since in all likelihood, many cases go unreported and unrecognized. The disease has a predilection as to sex, nationality and geographical habitat, age, and site of origin. The peak of fre-

quency of the disease is in the fifth, sixth, and seventh decades of life and the male is more often afflicted than the female by a ratio of 20 to one. Although no part of the world's population is unaffected by Kaposi's sarcoma, it is more prevalent in peoples of Eastern Europe and Northern Italy. The bulk of the statistics indicate that it affects Northern Italians most frequently, followed by Jews, Russians, and Poles; Negroes and Orientals are not immune, but cases are infrequently reported in these races.

Definition

Kaposi's sarcoma is a true but atypical sarcoma of blood vessel origin characterized by a cutaneous tumor which usually appears first on the distal portion of an extremity as a bluish-red macule which progressively forms other macules which slowly multiply and coalesce to form nodules and plaques. The lesion tends to be unilateral at the onset, later becoming bilateral and progressing to involve the trunk and finally, in about 10 per cent of cases, the viscera and mucous membranes. There are numerous case reports in which the secondary manifestations, such as lymphadenopathy, symmetrical swelling of the extremities and visceral involvement, appear first, to be followed in most cases by the cutaneous manifestations. Alteration in the hemogram is not marked or constant. The most commonly reported changes have been secondary anemia and monocytosis and, less frequently, eosinophilia and lymphocytosis. The presence of an increased number of abnormal mononucleated cells in Kaposi's disease as well as in mycosis fungoides has been reported. Others have reported Kaposi's sarcoma in association with mycosis fungoides[3,4] and with other malignant lymphomas such as Hodgkin's disease[5,6] lymphosarcoma,[7] and lymphatic leukemia.[8,9]

Case History

In September, 1958, a white female of 76 years was referred to the Hertzler Clinic with "a sore" on the plantar surface of the right heel present for nine months, two masses present in the groin for six weeks, and swelling of the right leg for two to three months. The patient was first seen by her local doctor 33 months prior to her admission to the Hertzler Clinic, with a small reddish-blue nodule on the plantar surface of the right heel. The lesion was excised at this time and a diagnosis of angioendothelioma made.

Two months later the patient was seen by a dermatologist and radiologist who diagnosed "a reticuloendothelioma, or an angioendothelioma, or possibly Kaposi's disease" and treated

3. Lane, C. G., & Greenwood, A. M., *Arch. Dermat. & Syph.*, 27:643-654,1933.
4. Lapowski, P., *Arch. Dermat. & Syph.*, 33: 170,1936.
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8. Sachs, W., & Gray, M., *Arch. Dermat. & Syph.*, 51:325-329,1945.
9. Wolf, I., *Arch. Dermat. & Syph.*, 48:566, 1943.

the lesion with 1600 r units, well windowed, at one sitting.

Several months later the patient consulted another group of physicians who did not arrive at any definite diagnosis but informed the patient of normal physical findings and advised her that she had been adequately treated.

The patient remained reasonably well with a residual sensitive area at the treated site which remained pigmented, until December, 1957, two years after onset. The involved area of the heel then ulcerated and she was again treated, this time with 2600 r x-rays and 9600 milligram hours of radium followed by 2500 r in five doses to a 2 cm. circle at 200 KV h.v.l, 1 mm. Cu at 50 cm. distance with a Thoreus A filter.

The ulcerated area did not heal and she was placed on additional treatment until August, 1958, with penicillin, streptomycin, and Parenzyme. From August, 1958, until she was referred to the Hertzler Clinic on September 11, 1958, she was treated with Furacin ointment locally and chloramphenicol systemically with no improvement.

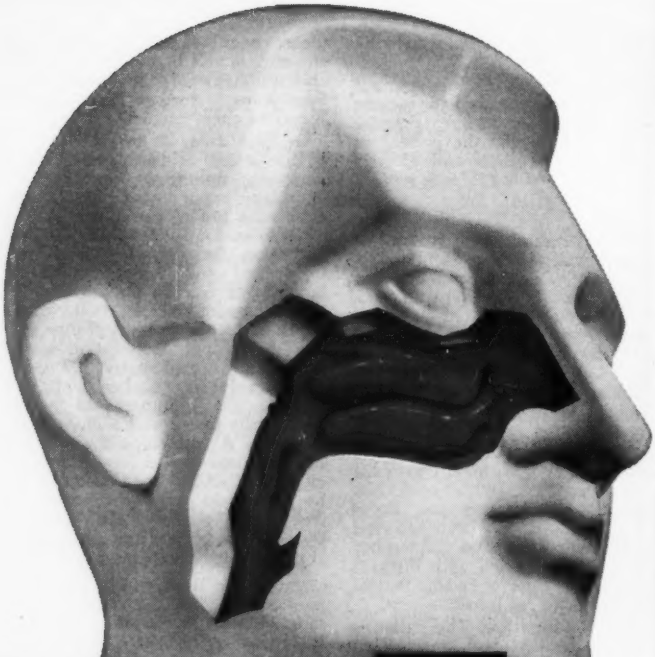
Physical Examination: The patient's temperature, pulse, and respiration were normal and she seemed in apparent good health for her age. The only positive physical findings were: minor cervical adenopathy, mild benign hypertension of 180/80, a matted adenopathy in the right groin measuring approximately 5 x 3 cm., a large deep sloughing ulcer measuring 2.5 x 2.5 cm., with a grayish floor covered by inflammatory exudate on the plantar surface of the right heel, and 2-plus pitting edema of the right leg and ankle.

Laboratory Procedures: Most of the laboratory findings were within the limits of normal as follows: hemoglobin 81 per cent or 12.5 gm., wbc. 6,850 with a normal differential with 3 eosinophiles; blood urea nitrogen 8.7; urinalysis normal; total protein 5.4, albumin 3.15, globulin 2.25 mgm./100 cc.; Kline negative, blood sugar 91. Bacteriologic examination of the ulcer; coagulase positive, staphylococcus aureus and B. proteus sensitive to chloramphenicol and albapenicillin. Heel x-ray: normal bony structure. X-ray of chest normal.

On September 30 an excision biopsy of the lesion in the right groin was performed under local anesthesia. The pathology report read: Metastasis of anaplastic tumor (sarcoma) in lymph node (Fig. 3). It was then decided to amputate the right leg between the upper and middle third of the tibia in order to rid the patient of an extremely painful ulcer that was apparently recalcitrant to proven methods of therapy. Amputation was advised and accepted by the patient. Accordingly on October 7, 1958, the right leg was amputated at the junction of the upper and middle third of the tibia. At the same time the right inguinal area was re-entered and cleaned of all tumor masses that could be found, in an effort to establish free lymph channels. The postoperative course was smooth and the stump healed by primary union.

Pathologic Report: The gross specimen consisted of the right leg amputated in the middle of the tibia. The leg measured 24 cm. in length. On the plantar surface near the heel was a deep ulcer (Fig. 1) 25. cm. x 2.5 x 1 cm. in size, the base of which was grayish in color and covered with an inflammatory exudate. No tumor was palpable. The muscles, blood vessels, and nerves of the leg were dissected and manifested no pathologic changes. Sagittal sections through the ulcer showed a crater 2 cm. wide and 1.5 cm. in depth. The wall of the ulcer was hard and whitish in color, but no invasive growth was seen in the surrounding fat tissue or bone.

Microscopic Report: The ulcer bed was covered with a layer of inflammatory cells and necrotic material (Fig. 2). There was extensive necrosis of the subcutaneous tissue. In the deeper layers tumor growth was noted consisting of spindle cells which varied greatly in size and form, and some of which had unusually large dark-



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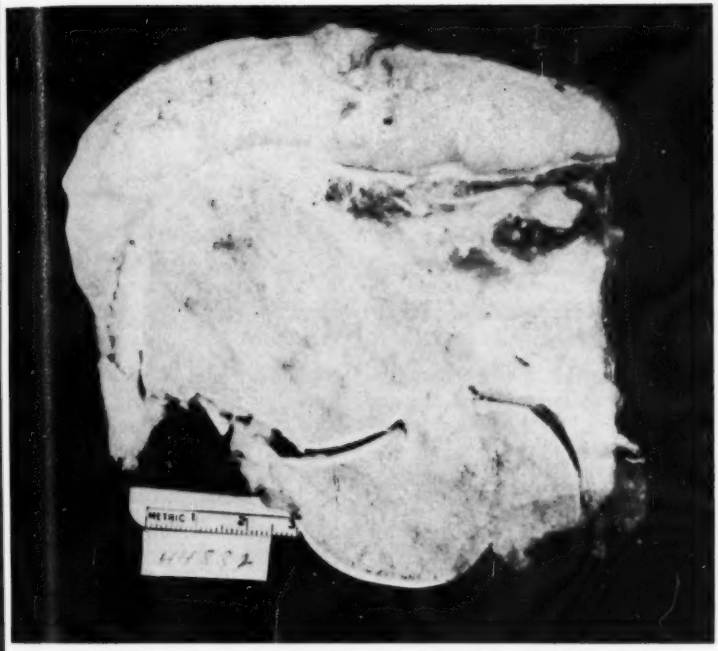

Figure 1. Kaposi's disease. Sagittal section of large heel ulcer.

stained nuclei. Tumor cells lined some of the blood vessels, invaded the surrounding tissue in small nodes and in strands, and reached the deeper layers of the subcutaneous tissues. Some infiltration with plasma cells was noted.

Diagnosis: Kaposi's sarcoma of the heel; deep ulcer with extensive necrosis.

Etiology and Pathogenesis

The etiology and pathogenesis of Kaposi's disease is still controversial. Many hypotheses have been proffered and none, as yet, have been universally accepted. Choisser and Ramsey have categorized the many etiologic theories into four main groups: (1) neoplasm, (2) infectious granuloma, (3) infectious granuloma with neoplastic potentialities, and (4) reticulo-endothelial hyperplasias. The most commonly accepted theory as to origin of the disease process is that it is pri-

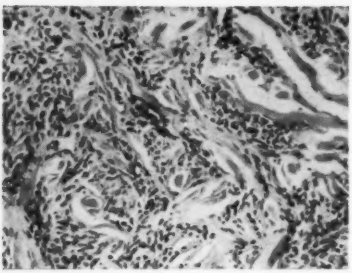

Figure 2. Kaposi's disease. Primary tumor.

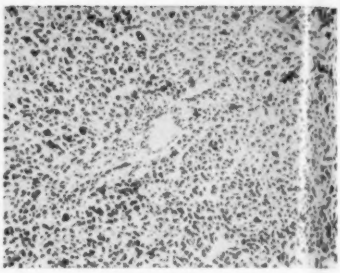

Figure 3. Kaposi's disease. Inguinal metastasis.

mary or secondary to chronic hyperplastic inflammation. Recent investigation,[10,11] however, lends some credence to the carcinogenic hypothesis, since it has been possible to induce similar angiosarcomatous lesions in experimental animals with injection of carcinogens such as azo dyes and hydrocarbons. The sex factor and the influence of sex hormones cannot be ignored since the sex incidence of the disease is so preponderantly male. Andervont's work in which he found a reduction of tumor induction after castration and testosterone pellet implantation, must be acknowledged. Hereditary vascular dysplasia must also be considered in view of the racial preponderance in Italians and Jews. The work of Greco and his group, who studied the disease in several members of the same family and came to the conclusion that the disease was of infective mycotic origin, must be recognized. Van Cleve and Hellwig also feel that there was an infective agent attacking the vascular and perivascular system with the lesions assuming neoplastic characteristics in predisposed subjects under certain conditions. Such are some of the theories as to etiology; it is not necessary to add: the etiology is unknown.

10. Andervont, H. B., & Dunn, T. B., *J. Nat. Cancer Jour.*, 7:455-461,1947.
11. White, J., & Stewart, H. L., *J. Nat. Cancer Inst.*, 3:331-347,1942.

Diagnosis

In a great many instances the first manifestation of Kaposi's disease is the pathognomonic bluish-red well-demarcated macule, easily diagnosed. If the cutaneous manifestation is either late or absent, the symmetrical elephantiasis of the extremities is fairly typical, especially in the presence of lymphadenopathy. A high index of suspicion is necessary if the disease is atypical, but the majority of cases are typical, and it is

with these that we are largely concerned.

Treatment

The most effective therapy for Kaposi's sarcoma is irradiation, especially if the lesions are multiple or the disease diffuse. Most lesions, and particularly the early ones, will respond to low voltage unfiltered roentgen therapy at weekly intervals. When the deeper structures, such as bones, lymph nodes, and viscera become involved, higher voltage—200 to 240 k.v. with cross-fire technic—is indicated. If leg edema is present, x-ray therapy should be conservative, since indications of impaired blood supply are present. Overtreatment may result in a chronic painful ulcer and even necrosis, infection, and gangrene.

The role of surgery, electric desiccation, radium, and nitrogen mustard are not too well documented in the literature. McCarthy and Pack utilized practically all modalities of therapy in their series of cases, including excision with scalpel and cautery; radium pack; external and interstitial radon; contact x-rays and 100 kilovolt, 200 kilovolt, and 240 kilovolt x-ray with all gradation of factors. They felt that in an early case, wide surgical excision can yield gratifying results. They believe, however, that surgery is contraindicated if the tumors are extensive or multiple or if edema is coexistent.

The treatment then could reasonably be outlined as wide surgical excision in a single early lesion and conservative doses of x-ray if the sarcoma is extensive or if edema is present. Radium therapy has been disappointing and nitrogen mustard of no value at all.

Prognosis

Contrary to Kaposi's original belief that the disease was rapidly fatal, the clinical course as a rule is long, since the progress of the disease is slow and characterized by remissions and exacerbations. Life expectancy of patients after the original diagnosis has been established is estimated at between five and twenty-five years with the average in the neighborhood of ten years. Death commonly occurs from intercurrent disease since Kaposi's sarcoma has its peak of frequency in the fifth to seventh decades of life. Death from Kaposi's disease is often the result of hemorrhage or emaciation due to visceral involvement.◀

J. Kansas M. Soc., 60:383-387,1959.

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Nosebleed: Radical Surgical Treatment

E. E. MIHALYKA, M.D., and THOMAS KRIEZAK, M.D.,
Parma, Ohio

►*A hypertensive man of 63 years with resistant nosebleed required radical surgery consisting of bilateral anterior and posterior ethmoid artery ligation. Transfusion of 12 pints of whole blood was required to maintain stable blood pressure. A radical approach to hypertension, but one worthy of further investigation.*◄

One of the most exasperating entities that any doctor has to deal with is the very frequent and common "nosebleed." Through the years many methods have been devised to attempt to help the patient suffering from painful and sometimes fatal nosebleeds. According to authorities,[1,2,3,4,5] nosebleeds can be treated by symptomatic medication, by cauterization with silver nitrate, by nasal packing, or by whole blood transfusion.

Following is the procedure we recommend for management of intractable nosebleed. First, the patient must be subjected to thorough diagnostic evaluation including hematologic study, complete physical examination, and hypertensive study. Prior to the nosebleed, the patient's blood pressure may be elevated, but afterwards and by the time the patient sees a physician the blood pressure is often almost within normal limits. One must not disregard hypertension as a causative factor in frequent nosebleeds.

When an individual presents himself with a "nosebleed," generally speaking, treatment can be conservative. In many instances, simply applying continued pressure for approximately 10 to 15 minutes to both external nares usually stops bleeding. If the initial conservative therapy does not seem to control the bleeding, bi-

1. Ballenger, H. C., & Ballenger, W. L., Diseases of the Nose, Throat and Ear, Lea & Febiger, Philadephia, 1943.
2. Portman, G., Surgical Technique of Otolaryngology, Williams & Wilkins, Baltimore, 1939.
3. Lewis, W. H., The Anatomy of the Human Body, Lea & Febiger, Philadelphia, 1942.
4. Anson, B. J., & Maddoch, W. G., Surgical Anatomy, W. B. Saunders Co., Philadelphia and London, 1952.
5. Lederer, F., Diseases of the Ear, Nose and Throat, F. A. Davis Co., Philadelphia, 1946.

lateral anterior nasal packings may be inserted. Posterior packs with bilateral anterior nasal packs may also be necessary. If, however, the patient continues to bleed through his packs, even through several pack changes over as many days, plus the additional help of whole blood transfusions, the physician must then resort to radical surgery. The following is a presentation of such a case:

Case Report

The patient is a 63 year old white man who entered the University Hospitals, Cleveland, for the first time on August 13, 1957, because of "nosebleed." The past medical history revealed no serious illnesses or operation. The patient has been a known hypertensive for approximately five years for which he has been treated for the past year with phenobarbital 0.016 Gm. three times a day. He has had one episode of epistaxis five months prior to this admission, and was treated at another hospital with anterior and posterior nasal packs as well as whole blood transfusion. Anterior packs were inserted during the day before admission.

Physical examination revealed a well developed, fairly well nourished white male who had bilateral anterior nasal packs in place. Blood pressure was 160/110, pulse rate 92/min., and respiratory rate 18/min. Temperature was 36.4°C. The eye grounds revealed a grade 2 retinopathy with slight increase in the tortuosity of the vascular vessels and there was arteriovascular nicking. No hemorrhage was noted. There was slight oozing from the bilateral anterior packs, but no active bleeding was observed. There was no bleeding into the nasopharyngeal area at this time. The rest of the physical examination was within normal limits.

Laboratory Data: The patient's hemoglobin was 13.2 grams (87 per cent); hematocrit 41 per cent; white blood cell count 9,700/cu. mm. with normal differential. Urinalysis revealed 1 plus albuminuria with occasional hyaline casts and 1 to 2 white blood cells per high power field. The Lee-White clotting time was seven and one-half minutes and 10½ minutes (second tube). Bleeding time was two minutes and 14 seconds. Prothrombin was 83 per cent. The chest x-ray was normal.

No further bleeding was noted in the morning and the packs were removed revealing punctate areas of bleeding bilaterally on the septal wall, a little less on the right side. Similar abnormalities were noted on the lateral wall of the left inferior turbinate. These bleeding points were cauterized with silver nitrate and bleeding ceased. That evening bleeding was again noted on the right anterior septal wall. This stopped with compression. Again, several small areas of the right septum were cauterized with silver nitrate. The patient was then treated with vitamin K, ascorbic acid, phenobarbital, penicillin and streptomycin.

There was no further bleeding noted until the fourth hospital day when his blood pressure, which had been running around 170/100, rose suddenly to 220/120 and profuse generalized epistaxis occurred. No anterior bleeding points could be found so a posterior nasal pack and bilateral anterior nasal packs were inserted. Nevertheless the patient continued to ooze slightly through the packs. Concomitantly the backflow of blood through the nasolacrymal ducts caused an irritative conjunctivitis. Once again, no bleeding was noted for the next 72 hours although the hematocrit dropped from 40 to 33 per cent and his hemoglobin dropped down to 11.4 grams.

On the sixth hospital day the patient again started to bleed actively and 500 cc. of whole blood was given.

The packs were removed and bleeding points on the septum were again cauterized. The patient was unable to take fluids because of the packs and was maintained on intravenous fluids throughout the course. For the next 48 hours the patient oozed blood slowly but without noticeable active bleeding.

On August 22, 1957, (the ninth hospital day) another posterior pack was inserted with a bilateral anterior packing with vaseline under general anesthesia. It was noted again that blood continuously oozed from the anterior portions of the packing. The hematocrit rose to 39 per cent after transfusion, but then suddenly fell to 39 per cent after transfusion, but then suddenly fell to 22 per cent and the hemoglobin fell to 8.2 grams. The white blood cell count rose to 13,800/cu.mm.

On the eleventh hospital day, August 24th, active bleeding occurred from the left side of his nose through the anterior and posterior nasal packs, and it was decided that surgery should be resorted to. Accordingly, he was taken to surgery where whole blood transfusion was started again. The procedure planned was ligation of the left anterior and posterior ethmoid artery.

Operation: The nasal and facial areas were properly prepared. The eyebrows were retained. A "Hockey Stick type" incision was made extending from the left supraorbital ridge down to the nasal suture line. The dissection was carried down and the periosteal elevator was utilized to reflect the periosteum lateralwards.

The Luango retractor was gently inserted until the left anterior ethmoid artery was isolated, ligated, and divided. With further dissection and lateral reflection of the periosteum of the eyeball itself and continual gradual deeper insertion of the Luango retractor, the posterior ethmoid artery came into view in the form of a "tenting" along the lateral wall of the nasal side of the eyeball approximately 1¾ inches deep. A pair of silver brain clips were placed across this vessel, one proximal and one distal. The vessel was not divided. The patient received three units of whole blood throughout this procedure.

The incision was closed and a Penrose rubber drain inserted and chlortetracycline ophthalmic ointment instilled into both eyes. An eye pack and dry dressings were applied to the left eye. Bilateral anterior and a posterior nasal packing was re-instituted following surgery. The patient withstood the procedure well and left the operating room in good condition.

During the next 36 to 48 hours he seemed to be doing well with no further bleeding. The hematocrit rose to 30.5 per cent after transfusion. Bleeding time was repeated and was two minutes, while the clotting time was eight minutes and platelet count was normal. Prothrombin time was 100 per cent. Electrolyte balance was maintained.

The anterior nasal pack was removed slowly over a period of two days. Forty-eight hours postoperatively, all packs were out and there was no bleeding. Twenty-four hours later, on August 27, at about 7:00 a.m. (the fourteenth hospital day) third postoperative day, the blood pressure suddenly rose to 140/90 and the patient had another epistaxis of approximately 150 cc. from the right side of his nasal cavity this time. Several small bleeding points were noted and cauterized with silver nitrate and adrenalin. Oxidized cellulose packs were inserted into the right anterior and posterior portions. Profuse epistaxis continued, however, on this side and it was decided that the right anterior and posterior ethmoid artery should be ligated.

Once again on this day, August 27, 1957, at 9:00 a.m. under general anesthesia a posterior pack was inserted and the right anterior nasal pack was re-inserted. No bleeding was noted from the left side throughout all of this. Once the right side packing was inserted, the vital signs remained fairly stable and the patient was again given blood transfusion. It was decided that the patient should be ob-

served. Towards the evening of August 27 the patient again passed large amounts of swallowed blood per rectum and it was decided because of persistent bleeding on August 28th, that the right anterior and posterior ethmoid artery ligation should be carried out.

Second Operation: On August 28, 1957, again under general anesthesia, the patient's right facial and nasal areas were properly prepared. An incision was made through the right supra-orbital ridge down toward the nasal suture line and dissected. The Luango retractor was inserted and the right anterior ethmoid artery was isolated, ligated, and divided. The periosteum of the right eyeball was elevated and reflected lateralwards and again the Luango retractor was inserted deeper into the orbit until the posterior ethmoid artery was revealed at a depth of 2 inches. The brain clips were utilized again and placed on the proximal and distal parts of the posterior ethmoid artery. A rubber drain was inserted and the incision was approximated and closed with No. 0000 black silk. One per cent chlortetracycline ophthalmic ointment was instilled into both eyes and a right eye dressing and patch was applied. Again the right side posterior and anterior packing was inserted. The patient withstood this procedure well and he left the operating room in good condition.

The blood pressure continued to hover around 170/100 all through the operative procedure and through the first postoperative day. On the second postoperative day, the blood pressure gradually dropped to 150/90 and there was a small amount of oozing through the pack posterior and anterior, but no active bleeding noted. The nasopharynx was clean and dry. On August 30, 1957, the second postoperative day (for the second surgical procedure), the packs were removed with no active bleeding noted at this time. During the next two weeks, the patient was followed very carefully and no further bleeding occurred. The hemoglobin returned to 11.6 grams, the hematocrit rose to 38 per cent and the rest of the laboratory values were within normal limits. The stools became guaiac negative and the patient was finally discharged on his thirty-second hospital day. He had received a total of 12 pints of whole blood and on the discharge day his blood pressure had been maintained at approximately 150/90.

Follow-Up: Now, one year later, the patient has been followed by his internist and monthly by us. His blood pressure has been maintained at 150/90, and there has been no further bleeding.◀

Ohio M.J., 55:1233-1234,1959.

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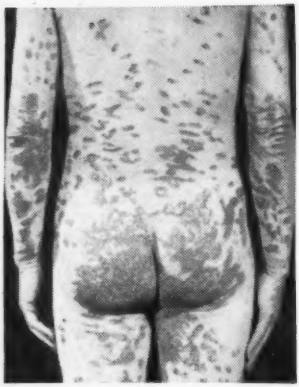
McDonald, D. F., & Orallo, M. O., *J. Urol.*, 81:534-536,1959.



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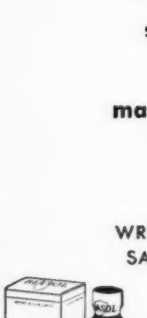

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Cancer of Rectum and Sigmoid Colon

JAMES E. McCLENAHAN, *Pittsburgh, Pennsylvania*

►This conference on surgical proctology was held at Mercy Hospital, Pittsburgh, on March 19, 1958, with James E. McClenahan, M.D., member of the senior staff in surgery at Mercy Hospital and associate professor of surgery at the University of Pittsburgh School of Medicine, as the guest participant.◄

This female of 74 years was surveyed about one and a half years before the present admission when she had crampy abdominal pain and "constipation." After this survey the patient was told that she had nothing but arteriosclerosis. The large bowel was not well visualized because she had no rectal sphincter, and even with the use of the catheter and bag the colon could not be filled with barium. The rectal sphincter had been lost as a result of multiple incisions for pruritus apparently associated with infection. This had happened many years previously. The patient's last admission before the present one was for bromide intoxication due to medication taken for dizziness. The patient had insisted on going home very early and at discharge had no symptoms other than the dizziness. She had one fecal impaction while in the hospital at that time which was broken up, giving her complete relief.

The chief complaint on the present admission was abdominal distention of six days' duration. The last bowel movement had been five days before admission. There has been associated nausea and vomiting. Physical examination on admission showed marked distention with tympany, and intestinal obstruction was suspected.

The day after admission the following note was made on the patient's chart: "Although I have been unable to see this patient's x-rays, this is the picture of an incomplete lower bowel obstruction. The patient's symptoms are less severe today than yesterday. She has not vomited since yesterday and her distention is less. Her bowels moved after the barium enema this a.m. The history is

Pennsylvania M.J., 62:1116-1120,1959.

suggestive of cancer of sigmoid or descending colon. Rectal examination revealed a rather extensive inflammatory process of the anus, apparently a fistula *in ano*. I was not sure that I did not feel a mass at the tip of the finger in the rectum. Sigmoidoscopy is certainly indicated. I do not feel that any surgery is indicated at present, but feel that oral intake should be limited to clear liquids and supplemented with intravenous therapy to keep the intake up to normal levels. If distention becomes worse or if vomiting recurs, tube decompression should be accomplished at once."

An attempt at sigmoidoscopic examination was not completely successful five days after admission, due to the presence of much fecal material in the lower bowel. A second attempt the following day was also unsuccessful. A week later sigmoidoscopic examination was reported as follows: "Marked scarring and granulation of the anal orifice The rectum was dilated and a sigmoidoscope passed freely up to 16 cm. The lumen of the bowel at that area was narrowed and small flecks of feces were seen to come through. No definite ulceration of the mucosa was seen."

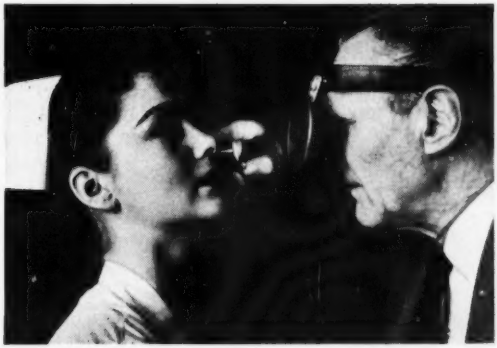
A flat plate of the abdomen taken on admission was reported as follows: "There is rather marked distention of the colon to the left of the mid-descending portion. In addition, there are several loops of moderately distended small intestine. The appearance is suggestive of a mechanical obstruction, with an incompetent ileocecal valve. A large round density, suggestive of a gallstone, is noted in the right upper quadrant. Osteoarthritic changes are evident in the spine."

A barium enema was performed the following day and the report was as follows: "The abdomen was distended. There was a large amount of air in the large and small intestine. The patient experienced pain and was not able to cooperate during the fluoroscopic examination. The barium did not go beyond the proximal sigmoid." Radiographic report: "There is an apparent, complete obstruction at the level of the proximal sigmoid. The marked distention of the colon is again noted. Several loops of the small intestine are also distended."

Three weeks after admission an anterior resection of the sigmoid colon was performed and an end-to-end anastomosis carried out.

Pathologic diagnosis was adenocarcinoma of the sigmoid colon. The tumor was a large yellowish-brown fungating mass which measured 8 x 6 x 3 cm. and appeared to occlude the entire lumen.

Postoperative course was uneventful and the patient was discharged 13 days after operation.



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References: 1. Personal Communication to Eaton Laboratories, 1959. 2. Spencer, J. T., in Conn, H. F.: Current Therapy 1954, Philadelphia, W. B. Saunders Co., 1954, p. 130.

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The discharge note read as follows: "This patient was admitted with an acute incomplete intestinal obstruction. A diagnosis of carcinoma of the sigmoid colon was arrived at with some difficulty because thorough examination was made difficult due to the absence of the patient's anal sphincter. At operation an obstructing adenocarcinoma of the sigmoid colon was encountered with metastasis to the liver. A palliative resection was performed with an end-to-end anastomosis.

DR. MARK M. BRACKEN: "Dr. McClenahan asked me some time ago whether this patient had been decompressed before operation. The surgeon who operated on the patient tells me that the patient decompressed herself before the operation.

"One very interesting thing that was found at the time of operation was a large metastatic mass in the patient's liver. A biopsy of this mass was not taken at the time of operation. Pathologically, the lesion in the sigmoid colon was found to be a mucinous adenocarcinoma and there were metastases in the regional lymphatics. Five years after this resection was done this patient was still living and well at the age of 78. The primary tumor in the sigmoid colon was a rather pedunculated, somewhat polypoid type. There were no other tumors in the portion of bowel removed.

"I would like to say a word in regard to the varieties of cancer in the large intestine in association with prognosis. Those that have an excellent prognosis are the pedunculated adenomas which have no invasion of the stalk. Even a sessile cancer which is not invaded down through the submucosa is associated with a good prognosis. It is only rarely that these tumors metastasize. Those that have a relatively good prognosis are the ones in which the cancer is limited to the wall of the bowel without any lymphatic spread. When there is lymphatic spread in the immediate area of the tumor, the patients have only a fair prognosis. This is speaking in terms of five-year survival. Individuals in whom the prognosis is poor to hopeless are those in whom the pathologic examination of the tumor reveals signet ring cells with mucin formation. Also included in this category are patients with extensive lymphatic spread of tumor and microscopic evidence of nerve sheath invasion. Thus in 1953 when this patient was operated upon she would have been considered a very hopeless case from the point of view of prognosis. The patient herself does not think so now as a recent letter from her would indicate."

DR. MCCLENAHAN: "I do not

have too much to say about the case itself as far as it was handled. In looking back on it one might say that the diagnosis should have been made one and a half years earlier had there been a proper follow-up. However, if one follows up everybody with a little bit of cramp in his abdomen from constipation at the age of 74, one is similar to the fellow who plans on taking out every person's appendix who has a pain in his belly. So I can see no particular fault in this case in regard to the follow-up. There is one thing that I would like to mention in this regard though; one finds that approximately 30 per cent of individuals who come to the hospital for an operation for carcinoma of the rectum or sigmoid colon have been treated for some other condition either by an internist or a surgeon or by both.

"In regard to the sigmoidoscopic examination, there are many people who cannot be sigmoidoscoped safely beyond the 16th cm. point. Roughly this is just about the junction between the sigmoid colon and rectum. I believe there is some misconception about sigmoidoscopic examinations. The idea is prevalent that if a proper sigmoidoscopic examination cannot be done without anesthesia it is wise to take the patient to the operating room and do the examination with anesthesia. It is true that because of spasticity some people cannot be sigmoidoscoped the full 24 cm. length, but I would like to warn you that the only patients I have ever seen perforate during sigmoidoscopic examination have been those under anesthesia.

"I see no record in the protocol that successive flat plates of the abdomen might have been made to indicate whether the patient was being adequately decompressed. I personally have great confidence in successive flat plates to see what progress I am making. The type of surgery used in this patient was excellent, I believe, in view of her age and pathologic findings at operation.

"Dr. Edwin Fisher, by use of the perfusion technique in aspirating blood from a segment of bowel removed because of intestinal malignancy, found malignant cells in one of the five patients examined falling under the classification Dr. Bracken has indicated to us as the best prognosis.

"The mucinous tumor such as this patient had is generally thought to be less malignant and is associated with a much more favorable prognosis than the ordinary adenocarcinoma. I do not believe that this is true. Histologically, the mucinous tumor may be a less malignant tumor, but there are really two types of mucinous tumor—the intracellular one and the extracellular one. The extra-

cellular mucinous tumor secretes the mucin as a lake carrying tumor cells and one must use extreme care in handling this tumor because the surgeon's hands may spread the mucinous substance which may contain the malignant cells. When the mucin remains within the cells, the prognosis is better. Once the mucin is released from the malignant cells the prognosis becomes very poor and the patients generally die within one or two years.

A number of years ago I removed an adenocarcinoma of the rectosigmoid colon and did an end-to-end anastomosis. At that time there was obvious metastasis to the left lobe of the liver. Five years later I had the opportunity to reoperate on this patient because of intestinal obstruction. At that time the metastatic tumor in his left lobe occupied the whole lobe but there was nothing in the right lobe of the liver. In the intervening five years he had worked and made a living for his family. He did die one year after the second operation. Some of these patients live for long periods of time even with liver metastases.

"A point that I would like to stress at this time is the very great improvement in handling patients with carcinoma of the rectosigmoid region in the past 20 or 30 years. Generally speaking, however, even today, according to Dr. Cameron of the American Cancer Society, 85 per cent of all patients with cancer of the rectum or sigmoid colon eventually die of that particular condition. Thus only 15 per cent of the patients are cured. In the group without metastases to lymph nodes, 75 per cent have a five-year survival rate. In those with nodal metastases at operation there is approximately a 37 per cent five-year survival rate. In other words, involvement of lymph nodes has a definite bearing on the prognosis of any particular patient. I think it is important to note that cancer of the colon is the most common form of malignancy in the male and the second most common form of malignancy in the female.

"I think it is important also that we should realize that 70 per cent of all tumors of the large bowel can be seen with a sigmoidoscope, and approximately 65 per cent of them can be felt with the index finger.

It has been found that 8 per cent of female patients with cancer of the rectum and sigmoid show evidence of concomitant malignancy in the ovaries, one or both.

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a good many years until Gallagher, and Dukes and Busey and later Cole were able to demonstrate that approximately 50 per cent of all recurrences of cancer of the large intestine in an anterior resection followed by end-to-end anastomosis were the result of implantation of viable cells broken loose from the tumor itself.

"Three types of operation are in use today in the surgical handling of cancer of the rectum and sigmoid colon. The first is an abdominoperineal resection, the second is the proctosigmoidectomy to preserve the sphincter, and the third is the anterior resection.

"From a prognostic standpoint it might be wise to consider three locations in which a cancer in this region may occur and study the lymphatic drainage from these regions. If the tumor is located in the anal canal or just within the anal sphincter, the lymphatic drainage follows the inferior hemorrhoidal artery and eventually goes to the groin. When the tumor is located about 4 or 5 cm. or even up to 10 cm. above the dentate line or above the internal sphincter, the lymphatic drainage is along the middle hemorrhoidal artery to the hypogastric set of nodes. If the tumor is at the peritoneal reflection or just above the peritoneal reflection, the drainage is upward—first to the mesentery of the sigmoid and then to the preaortic nodes, particularly around the origin of the inferior mesenteric artery."

MR. K. K. BUCK: "I have found slightly different figures from the ones quoted about 35 per cent nodal involvement—a reference in a recent journal of diseases of the colon and rectum concerning conservative versus radical treatment of carcinoma of the lower pole of the rectum and sigmoid. The argument is that if a patient has local node involvement at the time of operation there is an 80 per cent chance that the patient also has distant involvement. The author suggests therefore that conservative rather than radical surgery be used in such a case."

DR. MCCLENAHAN: "I feel that if one is going to do a good cancer operation he must be radical about the removal of the node-bearing areas. I do not see much excuse for an operation that is for cure unless one does a resection of the node-bearing areas. If there are known distant metastases then the operation is more a palliative one."

MR. BUCK: "Recent work by English investigators suggests that exfoliative cytology from rectal washings in a case of colon carcinoma is a valuable adjunct in the diagnosis of this disease. It is even claimed that this study has more value than a barium enema. How do you feel about the future use of this technique?"

DR. MCCLENAHAN: "Such a technique has been used only recently and by a relatively limited number of people. I believe that if a tumor is present it can usually be diagnosed by other means such as sigmoidoscopic examination, digital examination, or by the various methods of x-ray technique. I do not believe that exfoliative cytology will ever replace any of the diagnostic procedures we use today."

MR. BUCK: "I have found several references stating that any person who requires a barium enema should also be a candidate for sigmoidoscopic examination. What is your feeling about this, Dr. McClenahan?"

DR. MCCLENAHAN: "I feel that the sigmoidoscopic examination should invariably be done before the barium enema. For part of my reason for this I would refer you to the figure I quoted earlier when I said that approximately 70 per cent of all cases of cancer of the large intestine could be diagnosed by sigmoidoscopic examination. I do not believe that the patient should be subjected to the cost of a barium enema when the surgeon himself by the use of the sigmoidoscope can see the lesion with greater accuracy than the x-ray diagnosis can be made."

DR. S. AARON SIMPSON: "The only exception that we would take to what Dr. McClenahan has just said is that performance of the barium enema is slightly more difficult if the sigmoidoscopy has been done first."

MR. BUCK: "An article in the *Surgical Clinics of North America* recently stated that we have gone as far as we can go, surgically speaking, in decreasing the mortality rate in cancer of the colon. It claims that any future attempt to decrease this mortality would lie more along diagnostic than therapeutic lines. Would you care to comment on this statement?"

DR. MCCLENAHAN: "I agree with the statement. I believe that the future will stress more education of the public and of the doctors themselves. In the latter case the doctors should be educated to subject these patients to intelligent sigmoidoscopic examinations and intelligent handling of barium enemas and barium double contrast enemas."

DR. CHARLES C. ALTMAN: "Would it not have been a better plan to have done a colostomy on this patient in view of the fact that she already had an incompetent anal sphincter which fundamentally means that she had a perineal colostomy?"

DR. MCCLENAHAN: "In general, I would think that would be a good possibility, although one must remember that this woman was 74 years old. Older people are the group I find it most dif-

ficult to train to handle a colostomy. Apparently this woman had lived with her perineal colostomy for many years and so was accustomed to it and knew how to take care of it."

DR. BRACKEN: "In the past two years the department of gynecology and ours have seen several cases which were considered primary cancer of the ovary until the time of operation. At operation it was found that the primary tumor was in the large intestine and that the ovarian masses were metastases."

DR. MCCLENAHAN: "In my own experience that is not a very common association. However, we believe that from 8 to 10 per cent of lesions of the bowel in the female will show a tumor in the ovary."

DR. RUPERT H. FRIDAY: "In surgery on patients with rectal cancer is it routine to practice pelvic lymphadenectomy such as a gynecologist would do for cancer of the cervix? If hypogastric node involvement is found along the hypogastric artery, and if preaortic node involvement is found how far would you resect?"

DR. MCCLENAHAN: "If the preaortic nodes are involved without evidence of further metastases then I would do the typical extended operation with removal of the inferior mesenteric artery from the aorta with its node-bearing area and the inferior mesenteric vein at the level of the retroperitoneal third portion of the duodenum. I'd dissect downward from that area and then proceed with the rest of the operation. If there is node involvement in the hypogastric area, I would proceed to remove the lateral ligament as close to the pelvic wall as possible. Some surgeons are advocating stripping the presacral fascia. I have not done this.◀

Tinea Capitis: Measurement of Gonadal Radiations During Treatment

It should be noted that:

1. Tinea capitis is prevalent in epidemic form in many centers throughout the world.

2. The best way of quickly controlling these epidemics is by treating all patients resistant to topical and oral remedies with x-ray epilations.

3. Patients with Tinea capitis should be quarantined.

4. Roentgen rays when properly used have no immediate or late harmful effects to the scalp, the meninges, the brain, or the gonads.

Cipollaro, A., et al., *New York J. Med.* 59:3033-3040,1959.

Acute Leukemia: Remission After Treatment with Prednisone and 6-Mercaptopurine

In a boy of 17 with acute leukemia, complete remission of hematological and clinical symptoms occurred following therapy with prednisone and 6-mercaptopurine. The first symptom of leukemia had appeared 1 year prior to therapy. Upon admission, 200 cc. of whole blood was given and treatment with analeptic drugs and vitamins started. Four days later prednisone and 6-mercaptopurine therapy was started, initial dosage of the former being 30 mg. daily (later 80 mg. continued for 22 days), that of the latter 150 mg. daily throughout the hospital stay (reduced to 100 mg. daily after discharge). Three additional blood transfusions totalling 600 cc. were also given before discharge. The condition was critical for the first 15 days in the hospital, after which some food was taken, temperature decreased, and marked subjective and objective improvement became noticeable. Swelling of the lymph nodes, spleen and liver almost disappeared, and no trace of oral and throat infection remained. Color returned to normal, and weight rose from 126 to 143 pounds. Fever disappeared after six weeks. The patient was released 16 weeks post-admission and was in good general health and showed a normal blood picture when seen one month later.

Longo, P., *Policlinico (sez. prat.)*, 65:1639-1648,1958.

Precipitation Test For Systemic Lupus Erythematosus

A total of 41 serum precipitation tests using a solution of 12% *p*-toluenesulfonic acid in glacial acetic acid were carried out in 25 patients with confirmed systemic lupus erythematosus. Positive results were observed in 6 (25%) of the patients, and in 27% of the 41 serum specimens examined. No close correlation between the results of the tests and the severity of the disease could be made. Patients showed a similar incidence of positive results whether on steroid medication or not. The pattern of reactions observed indicate that the test is not specific for the disease but rather is an obscure serum reaction with a specificity approximating that of the C-reactive protein, serum mucoprotein, and similar test procedures.

Pearson, C. M., *J.A.M.A.*, 169:30-33,1959.

Early Diagnosis of Bronchogenic Carcinoma: Mass Roentgenographic Examination

A mass x-ray examination of 704,837 persons revealed bronchogenic carcinoma in 1.98 persons per 100,000. Among those over 40, incidence was 9.43 per 100,000. The cancer could still be treated by surgery in most of these persons. In 16, it appeared as an isolated mass, while in 6 the tumor was no longer operable. Apparently the optimal frequency of x-ray examination for constant control of bronchogenic carcinoma in a community is every year or two, but even this frequency will fail to reveal early enough the presence of tumor in some cases.

Giobbi, A., et al., *Lotta contro tuberc.*, 28: 1138-1144,1958.

Coccygodynia—100 Cases

In 85% of cases of coccygodynia the pain has its origin in either the sacrococcygeal joint or the muscles inserted into the lateral borders of the coccyx. In cases of severe trauma the pain is increased during defecation. If pain is sudden, trauma is the cause. Hip and leg pain accompanies the pain in the tail bone in many cases. In ¼ of the patients there was pain in the upper portion of the gluteal region or down the back of the thigh, and the piriformis muscle was spastic.

One researcher describes a very effective method of massage: With full-length insertion of the finger into the rectum, latero-posterior pressure will place its flexor surface horizontally across the surface of the levator ani and coccygeus muscles. The fibers of the piriformis are felt immediately beyond the sacrospinus ligament and are touched by the finger tip; now by a lateral motion the finger will stroke lengthwise that portion of the belly of the muscle lying within the pelvis. Massage is begun lightly, later pressure is increased. If pain is evoked, light massage is again used and pressure is increased as tenderness decreases.

If definite improvement does not result after the first 4 to 6 massages over a period of a week or 10 days, orthopedic or other consultation is suggested.

Most patients had an average of 6 treatments over 3 to 4 weeks. Foci of infection were treated when necessary. In a series of 100 patients, 62 treated only by massage, 80% were relieved of symptoms. Twenty-eight were treated by instructions for proper posture and by heat, with relief in 90%. Ten had massage and surgical removal of foci of infection, with relief of symptoms in 9.

Cooper, W. L., *J. Kentucky M.A.*, 57:178-181, 1959.

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Microdrepanocytic Disease

This anemia was discovered in 2 brothers, one 29 months old, the other 5½ years old. History of the family members revealed microcythemia and sickle cell anemia as hereditary diseases. The children presented symptoms of both microcythemia and sickle cell anemia, plus abdominal pain. Although a swelling appeared on the back of the hand of one child, he had no fever. The liver of the other child was enlarged and painful, bilirubinemia was high, the child was pale and had jaundiced scleras.

de Benedetti, R. G., et al., *Haematologica*, 43: 1109-1122,1958.

Cardiac Infarction: Armchair Treatment with and without Anticoagulants

A total of 307 patients with cardiac infarction, admitted within 3 days of onset and receiving treatment with and without anticoagulants, were classed into 3 groups according to severity of their condition. Of the 307, 15 died within 12 hours and are not included. Of the 112 treated in an armchair and given anticoagulants, 10% died, while of the 100 treated in an armchair without anticoagulants, 15% died. Of the 80 treated with bed rest and anticoagulants, 26% died. Death occurred in 6% of patients with typically severe cases having had armchair treatment with anticoagulants, in 16% of the same group given armchair treatment without coagulants, and in 22% of the same group having had coagulants and bedrest. Armchair treatment may lessen the burden on the heart muscles and the risk of pulmonary edema, and is effective prophylaxis against thromboembolic complications.

Helander, S., *Acta. med scandinav.*, 162:351-359,1958.

Virus Invasion: Biochemistry

The chain of events accompanying invasion of a living cell (Escherichia coli) by a virus (bacteriophage T_2) consists of the following:

1. The head of the virus has a core of nucleic acid (DNA).

2. The tail is tubular, with a spiraled protein casing.

3. An electrostatic attraction between the protein in this casing and chemical groups at the surface of the outer cell wall of the bacterium attaches the virus tail-first to the host.

4. A reaction between zinc in this cell wall and sulfur in the tip of the virus tail is followed by contraction of the protein sheath and injection of the core of the tail into the host cell.

Recent experiments indicate that passage of the viral DNA into the cell as associated with a change in configuration of the head from an elongated to a short, thick, form.

Editorial, *Drug Trade News*, 10:44,1959.

Patent Ductus Arteriosus in Adult Life

Patent ductus arteriosus, symptomless until middle life, then deteriorating rapidly and followed by angina of effort, may be due to increased left ventricular work. Of 12 men and 31 women aged 21 to 66 with patent ductus arteriosus and admitted to the hospital over a period of 10 years, one group of 40 had a left-to-right shunt. Of these 40, 24 had dyspnea on exertion, 10 left submammary pain, and three classical anginal pain. Twelve were symptomless, referred because of a murmur discovered on routine examination. The classical Gibson murmur was heard in 39 of the 40 patients, while nine had a mitral diastolic murmur of a large shunt. Seventeen of the 40 had cardiac catheterization, total pulmonary resistance being normal in eight, elevated to as much as six units in one patient only. Of the 36 in the first group treated surgically, 13 were symptom-free, 10 improved, and one unchanged after closure of the duct. Eleven of the 12 without symptoms before the operation remained so afterward, while dyspnea on exertion occurred in the remaining one after closure of the duct. No deaths resulted from the operation. Diastolic blood pressure rose in all and in most the heart size was reduced.

Fairley, G. H., & Goodwin, J. F., *Brit. J. Dis. Chest*, 53:263-277,1959.

Malignant Tumors of the Breast: Findings in 1,000 Cases

Of the 1000 patients studied, 11 were males. Pure adenocarcinoma, the most frequent form observed, was in the first or second stage in the majority of patients. A total of 81 had been operated on for benign breast tumor. In 48, a definite relationship between the tumor and a trauma to the genitals was found. Metastasis was found in 56% of those undergoing surgery. Early radical mastectomy was done whenever possible, followed by at least 1 cycle of x-ray therapy as soon as the operative wound had healed. Androgen hormones were given in large doses to patients with metastases, even if they were local or had been surgically removed. In operable cases, x-ray therapy and injections of large doses of cytostatic, chemotherapeutic and antineoplastic substances were made as soon as possible. Adrena-

lectomy and hypophysectomy were performed when acceptable to patients. Results, followed in 980 of the patients, showed the post-treatment survival rate to be 70% after two years, 42% after another 3 years. Later observation disclosed that 39% of the patients were still alive.

de Bernardis, F., *Acta chir. italica*, 14:647-684, 1958.

Cancer of the Lip

Excessive exposure to sunlight plays a part in the development of skin cancer in general, the light-complexioned, fair-haired being most susceptible to the harmful effects of actinic rays.

Lip cancers are found almost always on the lower lip and are uncommon in the female. Their relation to pipe smoking is conjectural. They are epidermoid carcinomas and usually of low grade.

Cancers are seldom confused with other lip diseases. Leukoplakic changes and keratoses can resemble early cancer. Leutic lesions are uncommonly seen. Other chronic inflammatory lesions usually respond promptly to appropriate local measures. Induration in the base of the lesion should arouse suspicion and any doubt can be readily resolved by submitting the lesion to biopsy.

Two major forms of treatment exist—surgery and radiotherapy. Each is regarded as equally curative, presuming that by surgery all the neoplasm is excised, and that in radiotherapy factors of distance, kilovoltage, filtration, fractionation and total dosage be carefully calculated. The local recurrence rate should be less than 5% for each form of treatment.

The major factors to be considered are the size and invasiveness of the tumor and the cosmetic and functional result to be anticipated. With radiotherapy of infiltrating tumors, minor or major defects of lip substance have been known to result. Superficial tumors can likewise be treated by either method, but when extensive are best irradiated.

In 10% of cases initially seen, cervical lymph node metastases will have occurred, while 10% will metastasize following treatment of the primary tumor (principally to the submaxillary nodes on the involved side, rarely to the submental nodes alone). The most effective means of dealing with these metastases is complete radical neck dissection.

The mortality from neck dissection is less than 3%, even in the advanced age group. Although radiotherapy for the treatment in neck metastases is distinctly a secondary procedure, the availability of supervoltage therapy may improve this status.

Schewe, E. J., Jr., *Missouri Med.*, 56:1361-1362, 1959.

Treatment of Ringworm of the Skin, Hair and Nails with Griseofulvin

Results indicate that griseofulvin is orally effective in the treatment of the common dermatomycoses including those caused by the Microsporin, Trichophyton and Epidermophyton varieties of fungi. It is not effective against tinea versicolor, candidiasis, moniliasis, thrush, and the deep mycotic infections (blastomycosis, sporotrichosis, coccidioidomycosis, actinomycosis, histoplasmosis, etc.). The usual adult dosage is one 250 mg. tablet four times daily. On this dosage itching of cutaneous ringworm lesions ceases within three to five days, followed by desquamation and a temporary brownish color of the affected skin (clearing in about three weeks). Clearing of thicker palmar and plantar skin requires about four weeks, of tinea capitis lesions four to six weeks. Although in onychomycosis new nail growth occurs in two to four weeks, treatment with griseofulvin is continued until the entire nail-plate has grown out (four to six months).

Of three illustrative cases, one of tinea cruris, another of onychomycosis due Trichophyton rubrum, and the third (in two brothers) of tinea capitis due to Microsporum audouini, all showed clinical cure without side reactions after treatment with griseofulvin for periods of from four weeks to four months. Toxic reactions to the drug have been few and minor in nature. Some patients experience headache or gastrointestinal distress during the initial period of treatment, this usually subsiding on continued administration. Occasionally a patient develops an urticarial eruption requiring discontinuation of the drug. Several patients with a history of penicillin sensitivity showed no adverse reactions to penicillium-derived griseofulvin. To date hematologic and visceral function tests done in patients receiving the drug have shown no abnormalities.

Griseofulvin is fungistatic, not fungicidal, requiring that treatment be continued until the affected parts are both clinically and mycologically negative. Wherever possible, mycologic confirmation of diagnosis is indicated before the drug is prescribed.

Weiner, M. A., & Gant, J. Q., Jr., *M. Ann. District of Columbia*, 28:423-424,1959.

Prevention of Recurring Rheumatic Fever

Prior to the advent of antibiotics the recurrence rate of rheumatic fever was reported as 50%. With the use of penicillin as a prophylactic agent, the rate has been reduced to 1 to 2%. Although penicillin can be used to prevent beta-hemolytic streptococcal infection by daily administration of small doses, and to effect prompt treatment of this infections with large doses, this program has been discouraged. It has been shown that only 50% of a series of recurrences had symptoms requiring treatment, while the remainder had no fever or sore throat, the infection being discovered only by culture after the recurrence. The method of continuous daily administration of penicillin orally, or by daily injection at definite intervals is advocated. When oral buffered penicillin G, 250 mg. tablets, and oral penicillin V, 250 mg. tablets, were given daily and intramuscular benzathine penicillin G, 1,200,000 units, once each month, the rate of recurrence was 1.5% for the year. Without this prophylaxis the rate was 19%.

The intramuscular route is best but the oral is more widely used due to reactions, pain of injection, or failure to keep appointment. When penicillin cannot be used, the usual practice is to give one or two 0.5 gm. sulfadiazine tablets, 100 mg. tetracycline tablets, or 100 mg. erythromycin tablets daily. Penicillin is bactericidal, sulfonamides essentially bacteriostatic.

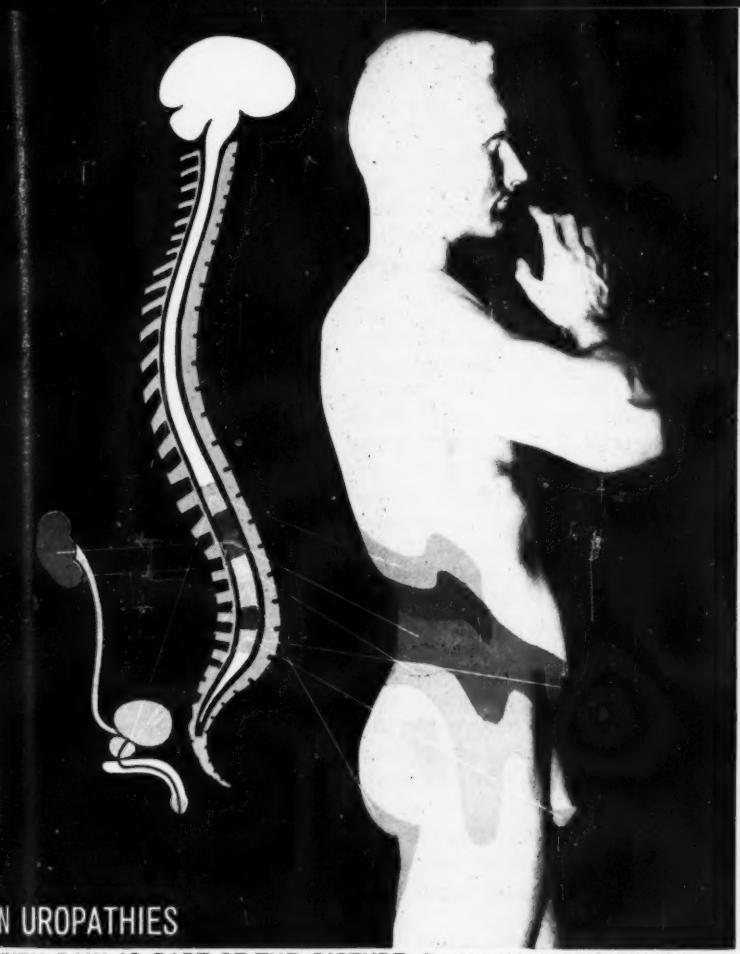
The most economical agent is the sulfonamides, next penicillin. In some instances the prophylactic drug is given for the remainder of the patient's life, in others for 5, 10, or 20 years. Since rheumatic fever is directly related to the beta-hemolytic streptococcus, an infection with this organism being capable of causing recurrence in a rheumatic fever patient, these patients must take prophylactic drugs so long as this possibility exists.

A rheumatic fever patient visiting his physician regularly, taking a prophylactic drug religiously, and observing the rules of good health, should never have a recurrent attack.

Berman, B. B., *Illinois M.J.*, 116:255-256,1959.

Oral Contraceptive

A combination of hormones consisting of 9.85 mg. norethynodrel plus 0.15 mg. ethinyl estradiol 3-methyl ether (Enovid) was administered to 830 women. A total of 8133 menstrual cycles was covered representing 635 woman-years and 4 studies. Regimen was 1 tablet daily from the 5th to the 24th day of the cycle. Practically 100 per cent contraception occurred if the regimen was fol-



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lowed. Contraception rate was proportional to the number of tablets missed. Significant abnormalities of the menstrual cycle were not noted, nor were there any adverse physiological effects. Habituation was not observed. Side reactions when they appeared included nausea, headache, and dizziness and declined to low levels after the first cycle. Restoration of involuted-postpartum uteri to normal size without hypertrophy, even after 30 or more cycles of medication, was noted in over 200 pelvic examinations. Although an inconsistent change in the degree of cervical erosion occurred, no pathological changes were observed in the vagina or other tissues, including the breast. Fertility was unimpaired in 86 patients withdrawing after one to 20 medication cycles. Weight increase occurred in 55%, an increased feeling of well-being in 39%, and libido changes in 42%.

Pincus, G., et al., *Science*, 130:81,1959.

Depression: Recognition and Management

The complaints in depression are many, greatly exaggerated, and do not yield to reassurance. They may range from persistent sleeplessness, loss of appetite, or constipation, to ideas of hopelessness or delusional ideas or cancer. Serious depression must be suspected when a patient makes pessimistic complaints out of all proportion to reality. The condition may be suspected when the complaints fail to respond to simple reassurance.

Regardless of depth, the complaints tend to follow a cycle, the patient returning to his usual outlook within a period of a few weeks to a few months. There is always a risk of suicide. Although learning a new philosophy of life may prevent subsequent depressions, few are able to do this and hence suffer repeated attacks.

The depressed patient must be kept active and interested. Although he may show a great deal of resistance, the attention and hopeful attitude of those making the effort are likely to have a much greater influence on him than he will admit. Neglect is only apt to cause resort to drastic measures to attract attention. The decision to hospitalize a patient is based on an estimate of the suicidal risk, although suicide is just as likely to occur in the hospital as at home. In itself, the hospital offers nothing of value except a more helpful environment. There is no substitute for human interest and enthusiasm in these cases, although the many drugs designed to stimulate or sedate can serve a useful purpose if used with discretion.

Goshen, C. E., *New York J. Med.*, 59:4392-4393,1959.

Acute Hepatic Necrosis: Early Detection by SGOT Estimation

Of 2 patients developing hepatic necrosis after iproniazid therapy, one had been treated for intractable angina and the other had taken part in a trial of the drug in the treatment of depression. In these cases a series of liver function tests were carried out to detect liver damage. Of 29 patients being given iproniazid, 9 showed elevated SGOT levels. Although the significance of this finding is uncertain, an elevated SGOT level should be accepted as presumptive evidence of early hepatic damage and the drug discontinued.

Pare, C. B. M., & Sandler, M., *Lancet*, 1:282-284,1959.

Radioisotopes Employed in Diagnosis and Treatment

I^{131} is the most prominently used radioisotope for the evaluation of thyroid disorders since its half-life is 8 days and, as a fission by-product of the atomic pile, it is readily available. I^{132} is used occasionally because its brief half-life (2.3 hours) affords certain advantages. An intake of more than 0.3 mg. of dietary iodine may give false results when thyroid evaluation is made. Decrease in I^{131} uptake may result from thyroid extracts, ACTH, sulfonamides, and certain tranquilizers. The usual tracer dose of radioiodine varies from 5 to 10 microcuries, 1/30th the maximum safe dose. The 24-hour uptake test is most widely used, although the thyroid clearance rate test is indicated in certain cases. With the uptake test, approximately 25 microcuries of radioiodine are administered intravenously, after which the rate of uptake in the thyroid is measured for 30 minutes. The rate of excretion is then measured and the clearance calculated. Uptake at the end of 24 hours may vary 35 to 55%. Another useful laboratory test is the use of I^{131} labelled triiodothyronine in measuring red cell capacity, an especially valuable procedure since it does not intefere with cell function.

Although various thyroid disorders may be differentiated and hyperthyroidism treated with I^{131}, it is contraindicated in pregnancy, particularly after the first trimester. Therapeutic dosage can be administered empirically (the average being 11 millicuries), or it may be calculated by multiplying

the estimated weight of the thyroid by the desired concentration of radioiodine in microcuries per gram. Therapeutic effects may not be noted for 2 or 3 months. Side effects such as thyroiditis are few and brief, and no damage to the parathyroids has been described. Excessive dosage may cause myxedema.

Thyroid cancer is best managed by surgery, although I^{131} may be useful in some metastatic types. For radioiodine treatment of this condition a moving scintillation crystal and recorder is valuable in judging response. Angina pectoris and intractable congestive heart failure sometimes respond to I^{131}. It has also been employed in fat absorption studies, renal function tests, and inhalation radiocardiography.

Co^{60} labelled vitamin B_{12} is useful in the study of pernicious anemia, (half-life 5.3 years, usual dosage 0.5 microcuries). Radioactive phosphorus is treatment of choice for polycythemia vera, most favorable results being observed in the simple type. It is safer to handle than gold because it has no gamma emission, and its half-life is 14 days as compared with 2.7 days for that of gold. Radioactive gold has been favored in the treatment of many neoplastic conditions, including those in the peritoneal or pleural space.

Wholey, M. H., *West Virginia M.J.*, 55:264-269,1959.

Selective Catheterization and Contrast Demonstration of the Left Ventricle of the Heart

Selective left ventricle catheterization and opacification provided valuable information in a series of pathologic conditions. In the method employed, the radial rather than the common carotid artery was chosen for insertion of the catheter since this route was found to be more practical, easier, and less dangerous. Catheterization was preferred to transthoracic puncture since it affords the advantage of permitting pressure measurements to be made with the catheter in position. It also allows time for careful consideration of the best site and method for injection of the contrast medium. Use of the catheter also permits the taking of pressure measurements during periods of rest as well as exercise. In the present series, the technique employed was varied according to the nature of each case. One drawback to the choice for the radial artery for insection of the catheter is the necessity of sacrificing this artery on removal of the catheter. If a larger artery is selected, the procedure of maneuvering the catheter through the aortic orifice will be more difficult.

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tip was employed. Cardiac activity was kept under observation with a cardioscope throughout the examination. After insertion of the catheter into the radial artery, it was first advanced as far as the aortic arch, then maneuvered carefully into the left ventricle through the ascending aorta and aortic valves. Pressure recordings were made along the aorta and in the ventricle. Contrast medium was injected in the amount of 0.75 ml. per kg. of body weight at the rate of 25 to 30 ml. per second. Film exposures were started simultaneously with the injection, six films per second being taken for five to six seconds. Views were taken in two planes at right angles to each other.

The pathologic conditions in which this method provided valuable information were:

1. Ventricular septal defect with left-to-right shunt.

2. Atrial septal defect involving the inferior portion of the septum.

3. Aortic valvular stenosis.

4. Subaortic stenosis.

5. Aortic valvular incompetence.

6. Mitral valvular disease with insufficiency.

7. Combined left heart valvular disease.

8. Pathologic lesions in the ventricular wall (tumors, fibroelastosis.

The method described was the only one capable of producing an exact diagnosis in the cases of subaortic stenosis and various combinations of valvular disease of the mitral and aortic orifices. It is not believed to be a more dangerous procedure than thoracic aortography or catheterization and selective demonstration of the right ventricle.

Hanson, H. E., Jonsson, G., & Karnell, J., *Acta radiol.*, 52:33,1959.

Salivary Gland Tumors

Benign mixed tumors are the most common salivary gland tumors. They are characteristically single, freely movable, and have a round smooth surface. The size varies, some becoming very large. Few cause any associated symptoms. When properly treated the patient is cured.

In the early stages no reliable clinical signs are present to indicate whether the tumors are benign or malignant. A lump at the angle of the jaw warrants investigation at the earliest date. As in any other tumor surgery excision is a necessity. It is rare that the seventh nerve need be damaged or sacrificed, even with malignant tumors.

Editorial, *Med. Ann. Dist. of Columbia*, 28: 349,1959.

Doctors and the Law

CHARLES J. FRANKEL, M.D., L.L.B., *Editor*

►*Is doctor guilty of malpractice if, while attempting to inject tetanus antitoxin into patient's spinal canal, the needle breaks? Is he guilty of malpractice if he leaves the broken portion of the needle in the patient's body for twenty-seven days?*◄

These questions were before the Missouri Supreme Court in 1958 (*Williams* vs *Chamberlain*, 316 S.W. (2d) 505). Defendant doctor had been treating plaintiff's head cut for a little more than a week. When she complained of stiffness in her neck and jaw, she was hospitalized. After various laboratory tests and a skull X-ray, her condition was diagnosed as tetanus. Plaintiff was placed in an "arched" position to separate the vertebrae and defendant attempted to inject tetanus antitoxin into her spinal canal. When the needle had been partially inserted, plaintiff gave a sudden, unexpected jerk, causing the needle to break before it had actually gone into the spinal canal and leaving the proximal end of the broken portion about one-quarter of an inch below the skin's surface. No attempt was then made to remove the broken portion of the needle, a piece perhaps six centimeters in length. Plaintiff remained acutely ill with tetanus for several weeks. When her condition improved, X-rays were taken, revealing the broken portion of the needle, and it was removed. Plaintiff now suffers from a slight stiffness in the neck, a somewhat limited grip in her right hand, a little instability when bending "too far" to the right and a slightly diminished reflex in her right foot.

The Court said the breaking of a hypodermic needle in the course of medical treatment does not, in itself, bespeak negligence. Needles may break because of an unobservable and unknown defect in the needle or a sudden movement by the patient, as well as from an improper usage or method, and the break may occur despite all the skill and care a

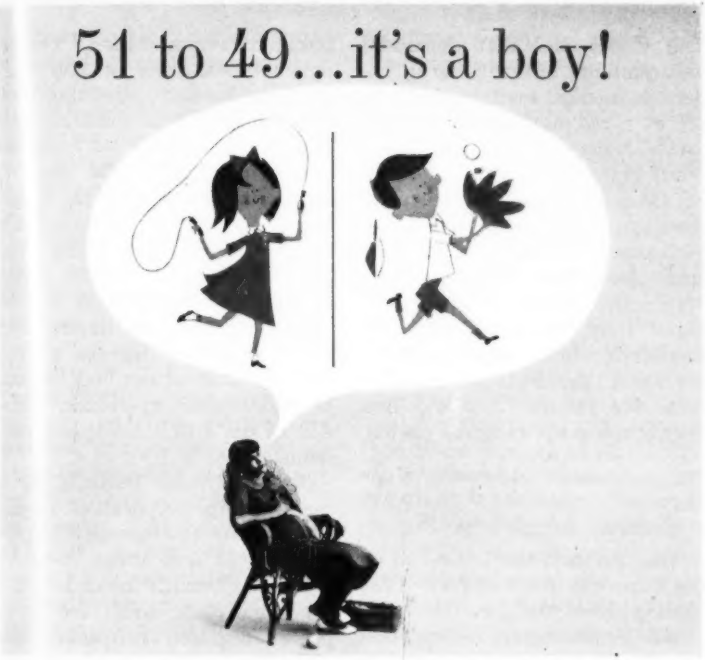
doctor may use. Plaintiff's principal contention was that defendant was negligent in leaving the piece of broken needle in her back for approximately twenty-seven days. The fact that the piece of needle might cause pain is not controlling. Defendant was negligent only if he was not justified, as a matter of medical judgment, in waiting as he did before removing the fragment. Any negligence in this connection can be established only by expert testimony. There was no expert testimony that it was negligent of defendant to wait before removing the fragment. There was, on the other hand, expert testimony that, in view of plaintiff's serious illness, it was better practice to allow the piece of needle to remain in her back until there was an opportune time to remove it, and that twenty-seven days was not too long a time to have left it. There was also medical evidence that plaintiff's present condition was probably caused by the original head injury and a resulting blood clot, and not by the presence of the broken needle fragment. There is nothing in this record, said the Court, to support a finding that defendant was guilty of malpractice.

►*Can plaintiff in malpractice case use defendant doctor's extra-judicial statement as the expert testimony necessary for submission of case to jury?*◄

The Supreme Court of Alabama passed on this question in 1958 (*Pappa* vs *Bonner,* 105 So. (2d) 87). Defendant performed a tonsillectomy on plaintiff, a boy about five years old. Defendant operated the hospital in which the tonsillectomy was performed. After the operation's completion, about noon, plaintiff was returned to his hospital bed and his parents were told to let him sleep the ether off. No doctor or nurse entered plaintiff's room until between 4:30 and 5:00 p.m. The Court said there was sufficient evidence to support a finding that the child suffered from anoxia immediately after the operation due to a blockage in his throat which permanently damaged his central nervous system. The issue was whether there was an expert testimony that the anoxia, and the resulting damage, was proximately caused by failure of doctors and nurses to attend him during the post-operative period.

Plaintiff contended the necessary expert testimony was provided by a statement made by defendant when he returned to the hospital at 7:00 p.m. He said that plaintiff should have been constantly checked and that his condition was due to the hospital's failure to give him adequate care.

51 to 49...it's a boy!



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1. Projection from Vital Statistics, U.S. Govt. Dept. HEW, Vol. 48, No. 14, 1958, p. 398.
2. Modell, W.: Drugs of Choice 1958-1959, St. Louis, C. V. Mosby Company, 1958, p. 247.

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The Court said that defendant was qualified to testify as an expert on medical matters. A plaintiff in a malpractice action may establish his case by expert testimony of the defendant doctor and his extra-judicial admissions have the same legal competency as direct expert testimony. The Court said defendant's extra-judicial statement furnishes some evidence from which a jury could reasonably infer that plaintiff's condition proximately resulted from the failure to attend him during the post-operative period.

►*Is a statute requiring certification of persons representing themselves as psychologists constitutional?*◄

This question was passed on by the Supreme Court of New York County, New York, in 1959 (*National Psychological Association for Psychoanalysis, Inc.* vs *University of the State of New York*, 188 N.Y.S. (2d) 151). Article 153 of the Education Law provides that no person shall represent himself as a psychologist unless he is certified and registered. The article provides that a person represents himself as a psychologist "when he holds himself out to the public by any title or description of services incorporating the words 'psychological', 'psychologist' or 'psychology', and under such title or description offers to render or renders services to individuals, corporations, or the public for remuneration." The article sets standards of age, character, citizenship, education and experience for certification and requires passage of an examination in psychology, the scope of such examination to be determined by a board of examiners in psychology. The article also provides that, for certain period of time, the examination may be waived as to those having doctors or masters degrees in psychology and prescribed periods of professional experience. Violation of the article is made a misdemeanor.

The suit was brought by a membership corporation organized for the advancement of psychoanalysis and three members thereof. Plaintiffs conceded that the State may, under the police power, regulate occupations that affect the public health or welfare and that their specific fields of psychoanalysis and psychotherapy, if not every branch of psychology, are subject to such regulation. They contended, however, that Article 153 is unconstitutional as a violation of the due process and equal protection clauses of the state constitution because it fails to define "psychology." The Court said that Article 153 does not prohibit anyone from practicing psychology or rendering psychological services; it merely bars a person from representing himself as a psychol-

ogist unless his qualifications are approved in accordance with its provisions. It is a certification, rather than a licensing, law. Since the article does not regulate the practice of a profession, but merely provides accreditation for those holding themselves out to the public as rendering services under a specific designation, the failure to define the designation is not fatal. In determining whether a person has complied with the law, the question is not one of whether he is a psychologist or rendering psychological services. The question is whether he holds himself out to the public under any designation using the words "psychology," "psychologist" or "psychological" and renders any services under such designation for remuneration. For that purpose, it is sufficient under the law that the words are used, whatever they may mean.

Plaintiffs further contended that the article, as written, is not reasonably calculated to accomplish its purpose of protecting the public from charlatans and unqualified persons representing themselves as psychologists. The Court said it was not within its province to weigh the probabilities of the article's success in stamping out the evil. It is sufficient that certification should, in some degree, make available to the public some information as to the qualifications and training of those offering to render services as psychologists.

►*Is an anesthetist who allegedly administered a spinal anesthetic in the region of the twelfth thoracic vertebra guilty of malpractice? Can the surgeon be held liable for the anesthetist's alleged malpractice?*◄

An Indiana appellate court passed on these questions in *Huber* vs *Protestant Deaconess Hospital Association of Evansville*, 133 N.E. (2d) 864 (1956). Since the trial court had directed a verdict for defendants, the evidence had to be considered in the light most favorable to the plaintiff. When defendant anesthetist administered a spinal anesthetic to plaintiff in preparation for an appendectomy, pain shot into his head and he felt as though he had been hit by something. Following the administration of the anesthetic, plaintiff became nauseated, his right foot and leg became paralyzed and numb, he was unable to urinate and had to be catheterized. The same condition that prevailed as to the leg existed on the right side from the waist down, both front and back. These conditions still existed at the time of the trial in a moderated form. Prior to the administration of the spinal anesthetic plaintiff had never had anything wrong with his back or the right side of his body.

There was expert testimony

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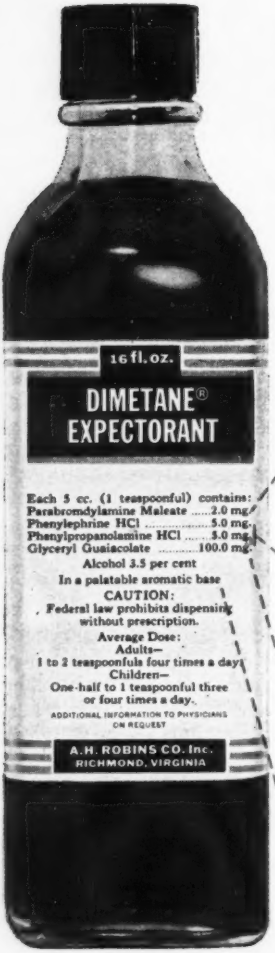

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that in administering a spinal anesthetic the needle should be inserted between the second and third lumbar vertebra of the spine. The evidence was conflicting as to where defendant anesthetist inserted the needle. Defendant anesthetist testified the needle was inserted in the proper place. A doctor who testified about his examination of plaintiff stated that plaintiff had pointed to a place in the region of the twelfth thoracic vertebra where he believed the needle had been inserted. Plaintiff's parents testified that after the operation they saw a red spot to the left of his spine and a short distance below his shoulder blade.

There was also expert testimony that plaintiff had sustained a partial conus injury on the right side which produced an anterolateral cordotomy from the twelfth thoracic vertebra and that this could not have occurred if the needle had been inserted in the proper place.

The Court said that there was sufficient evidence from which a jury could reasonably have found that defendant anesthetist was negligent in having made the injection for the spinal anesthetic too high and that the case should have been submitted to the jury.

Plaintiff contended that defendant surgeon also was liable for any negligence of defendant anesthetist. Defendant anesthetist was assigned by the hospital to administer the anesthetic after defendant surgeon's request that he be furnished a hospital anesthetist. Defendant surgeon was in another room sterilizing his hands while the anesthetic was being administered. The Court said there was no evidence on which a reasonable inference could be based that the anesthetic was administered under the direction and control of defendant surgeon. The cases uniformly hold that a surgeon is not liable for an anesthetist's negligence unless the negligent acts are committed under such circumstances as impose a duty on the surgeon to correct the anesthetist. No such circumstances exist here. The Court said that holding defendant surgeon liable would establish a rule of law making a doctor liable for all acts and recommendations of specialists he has consulted or whose services he has used even though such acts and recommendations are in no way subject to his dominion and control. In this age of specialization in medicine, courts have a duty to apply rules of law with an intelligent understanding of the developments in medicine and surgery.

►*Can a malpractice insurer be held liable for expenses incurred by insured doctor in settling malpractice*

action for alleged assault, if policy did not apply to injuries arising out of criminal acts?◀

This issue was before the U.S. District Court for the Eastern District of Missouri in 1959 (*Sommer* vs *New Amsterdam Casualty Company,* 171 F. Supp. 84). The policy issued by defendant to plaintiff, a psychiatrist-psychoanalyst, provided that defendant would pay "on behalf of insured all sums which insured shall become legally obligated to pay as damages because of injuries arising out of malpractice, error or mistake in rendering or failing to render professional services" and would "defend any suit against the insured alleging such injury . . . even if such suit is groundless, false or fraudulent." The policy also provided that it did not apply "to injury arising out of a criminal act." An action was brought against insured charging that he had committed an assault on the plaintiff in that action by placing him in a sanatorium for the mentally ill. The insurer refused to defend insured in the action. Insured subsequently settled the case; the present action is to recover attorney's fees and other expenses incidental to settling the case.

Defendant moved for summary judgment. It contended that, since the plaintiff in the action against insured alleged an assault and "assault" connotes a crime, it did not owe the insured either the duty to defend or to pay. The Court said an insurer has a right to interpret its policy and determine whether it will or will not defend and whether it will or will not pay, but such decision is not binding upon courts. The Court also pointed out that an assault is not necessarily a criminal act. An intent to do harm is at the basis of the criminal act of assault.

The Court said there was a further reason why the motion for summary judgment should not be granted. The policy insures against injuries arising out of "malpractice, error or mistake in rendering or failing to render professional services." The Court said the word "malpractice" includes the performance of criminal acts and that the words "error" and "mistake" could also embrace an assault. If there are provisions in an insurance policy which attempt to exempt the insurer from risk arising from certain conditions, which in fact exist and are known to insurer, and if the provisions, if given effect, render the policy inoperative at its inception, such provisions are invalid.

In other words, can defendant offer plaintiff a policy protecting him from damages for malpractice (which embraces as-

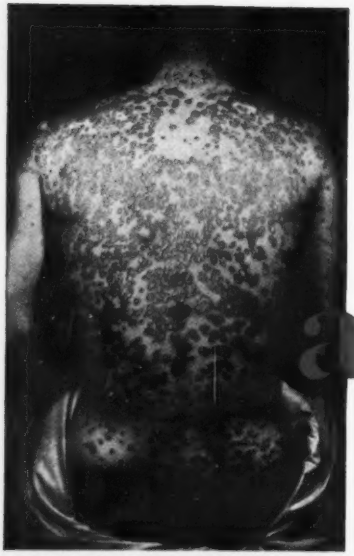
sault) in one breath and then, in the next breath, turn around and exempt assaults? If that be the case, what has the insurer given the insured? Certainly the insurer should not receive a premium for a policy for malpractice and then turn around and exclude the very thing for which it took the fee.◀

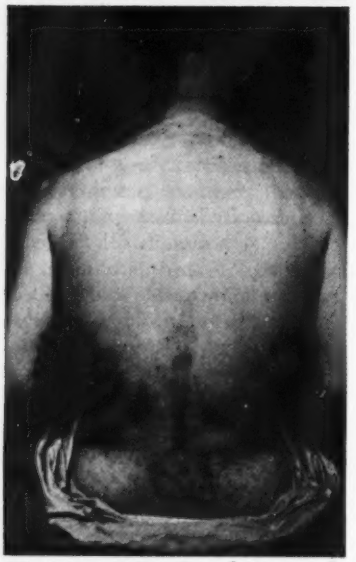
Malabsorption Syndrome: Xylose Test

In 114 normal subjects the 5-hour urinary excretion of xylose after an oral dose of 25 gm. was 5.7 gm. A finding of less than 3.0 gm. is presumptive evidence of malabsorption. To determine the accuracy of the xylose test in detecting malabsorption, results were analyzed among 34 patients with diarrhea, glossitis and megaloblastic anemia. The 5-hour xylose excretion was less than 3.0 gm. in 29 of these 34 subjects. Of the 5 excreting more than 3.0 gm. in 5 hours, 2 did not have sprue and 3 mild or borderline cases. According to these results, the xylose test alone detected 29 out of a possible 32 cases of malabsorption, an accuracy rate of 91%. Of 20 subjects with low xylose excretion placed on a fat-balance regimen for a period of 12 days, all exhibited steatorrhea, i.e., excretion of 6.1 gm. of fecal fat daily. In iron deficiency, sickle-cell and aplastic anemia cases, xylose excretion was found to be uniformly normal. The test was also normal in 2 patients with hepatic cirrhosis and borderline in a third patient with this condition. Low xylose excretion in the face of normal results with other absorption tests was encountered in 2 of 3 cases of pernicious anemia in relapse and in 2 of 9 cases of megaloblastic anemia of pregnancy. In 49 patients with sprue, mean xylose excretion was 1.4 gm. in 5 hours. Intravenous administration of xylose to normal persons and to patients with sprue resulted in excretion of 11 gm. in 24 hours in all subjects.

The xylose test is simple, reproducible, accurate and causes a minimum of inconvenience. In normal renal function, blood samples or venipunctures are not required. The simplicity and accuracy of this test suggests its widespread use in the diagnosis of malabsorption syndrome.

Butterworth, C. E., Jr., et al., *New England J. Med.*, 261:157-164,1959.





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*Combes, F. C.: New York State Jrl. Med., 54:13 Pt. 1945, (July) 1954.
*Fox, C. F.: The Treatment of Common Skin Diseases. G.P., 20:1 (July) 1959.
**Rosenthal, T.: Management of Psoriasis, In Press.

The Doctor Builds His Estate

Prepared monthly by the Research Department of Bache & Co., 36 Wall Street, New York 5.

▶*These monthly articles point out one method by which the physician may overcome the handicap imposed upon him by taxes on the bulk of his income at normal rates, as opposed to the capital gains tax open to many business men. One solution is systematic investment of current income in securities.*◀

One of the investment community's favorite measuring sticks for common stocks is the price-earnings ratio, or multiple, the price of a stock divided by the earnings per share. Multiples are a handy way to gauge the value the market is currently placing on a company's earning power, particularly since it is easy to compare it mathematically with the multiples being placed on leading stock averages, on companies in the same industry and on companies with similar earnings records.

As a general rule, investors pay higher multiples for issues with greater growth prospects, lower ones for stocks whose growth is interrupted by the fluctuations of the business cycle and the lowest ones for situations where growth is not expected or where the earnings are either regarded as non-recurring or are too new to be accepted at face value.

A prime example of a high multiple growth stock is Minnesota Mining & Manufacturing, now selling at over $170, or something like 50 times estimated 1959 earnings of $3.35. (The Dow Jones Industrial Average, by means of comparison, sells now, after a long rise, at about 18 times 1959 earnings.) U.S. Steel probably is as good an example as any for the second type, where the company's good long-term growth record is interrupted periodically by recessions. The stock, selling just over $100, earned an estimated $5.00 in strike-torn 1959.

American Motors is a clearcut example of the third case, one in which earnings are too recent to be fully accepted at face value by the market. The company

earned $10.14 a share last year, and sold during much of the year for $30-50, during which time the $10.00 earnings estimate was widely publicized. Thus, the astounded market (American only earned $4.65 in the previous year, and was in the red in the four previous years) was only paying 3-5 times earnings for much of the year, in contrast to 18 times earnings for GM and about 15 times for Ford.

This month, we are discussing three stocks selling at multiples we regard as too low. The fact that multiples do change from time to time offers the patient investor opportunities for substantial profits. We think such profits are distinct possibilities in Smith-Douglass Chemical, James Lees and J. P. Stevens.

Smith-Douglass

An important producer of fertilizers and animal feed supplements, Smith-Douglass markets its products primarily in those areas of the South and Midwest where tobacco, cotton, peanuts, corn and wheat are grown. Of its products, mixed fertilizer and fertilizer materials are by far the most important, accounting for nearly 70% of total volume. Secondary in importance are nitrogen and phosphate products. An important by-product is silica fluoride. To process its products from raw material to finished stage, the company operates 11 manufacturing plants with an overall annual capacity of 925,000 tons.

Last year, Smith-Douglass' domestic sales gain was equal to, if not greater, than the industry-wide increase in consumption in most of its trade areas. A decline in export sales was experienced, but this was due primarily to unsettled political and economic situations in the countries in which Smith-Douglass' products are sold. In spite of the dip in overseas business, the company turned in the best earnings performance in its history. Sales of $45.9 million compared with $39.9 million in 1958, and net income rose from $1.45 to $2.75 a share.

In the first quarter of the present fiscal year, beginning August 1, 1959, this upswing continued: sales increased 31% to $9.5 million, while earnings jumped 80% to 63¢ a share, by far the best first quarter the company has ever had. In view of this fine start, an earnings forecast of around the $3.00 mark seems reasonable for the full 1960 fiscal year. Of course, the farm chemical business is highly seasonal and heavily dependent on weather conditions as well as on the Government's farm program, neither of which can reliably be predicted. However, barring any acute disturbances of this external nature, it seems likely that

in the 1961-62 period the company's earnings potential should further improve to a $3.50-$4.00 range.

There are two major explanations for Smith-Douglass' dramatic operating improvement. First, almost all producers of fertilizers profited last year by a substantially augmented demand due to relatively more favorable weather conditions, higher farm income and generally firmer prices, than those of the preceding year. Moreover, farm chemical makers benefited from a 1959 change in the Government's farm program which restored some acreage, particularly in the corn and cotton growing areas, for planting purposes.

The second cause of the company's improvement can be traced to internal rather than external factors. In May of 1957, Smith-Douglass acquired for $500,000 the stock of Texas City Chemical Company, which had invested $6 million in fertilizer and feed supplement facilities but was unable to operate profitably because of a heavy debt burden. Following a Federal court reorganization which involved a reduction of the debt structure, Smith-Douglass took over the defunct company and commenced a capital improvement program designed to restore Texas City to a profitable position. This program, of course, required some time and money to show results; and in its 1958 fiscal year, Smith-Douglass incurred a loss of 43¢ a share on the new operations. However, by June 1958, Texas City reached the break-even point, and since then has been in the black. This turnabout accounts in an important measure for last year's improvement and indicates still further gains in 1960.

A third element of future interest is the merger with Smith Agricultural Chemical Company on September 15, 1959. At the time of the merger, Smith Chemical had a book value of $3.2 billion and sales in excess of $10 million. The company's area of operation was in Ohio, Indiana and Michigan. In the early 1950's Smith Chemical earned in the vicinity of $300,000 to $500,000 a year, but had not in recent years been more than modestly profitable. However, depreciation and other non-cash charges had been throwing off about $240,000 a year, an important element in evaluating the company's worth. While the newly acquired company is not likely to make any important addition to income in the near future, the acquisition will strengthen Smith-Douglass' position in Ohio, Indiana and Michigan—states in which it has not previously been effectively represented. Further, under the guidance of Smith-Douglass' more

SMITH-DOUGLASS

Recent Price	25½	Capitalization (7/31/59)	
Dividend	$1.20	Long term debt	8,655,722
Yield	4.7%	$5 Cum. ($100 Par pfd.)	23,483
1959 Price Range	29⅜-22⅞	$5 Second Cum.	13,722 shs.
Traded	N.Y.S.E.	Common $5 Par	944,288 shs.*

*11.4% Closely Held

aggressive merchandising techniques, the new unit could develop into another respectable source of profits.

Smith-Douglass' financial condition is quite satisfactory, especially since the company's debt structure was recast in 1958, permitting a considerably easier schedule on its debt. Last year expenditures for property and plant acquisitions totaled $1.8 million, down from almost $2.0 million the year before, and it is expected that capital expenditures will continue to taper off. In view of this, an increase in the dividend rate seems likely. (Dividends have averaged about 51% of earnings in the past five years.)

In sum, the shares of Smith-Douglass, while somewhat speculative because of the vagaries of weather and politics, appear undervalued at 9 times 1959 earnings and only 8 times forecast 1960 net. We recommend purchase, therefore, for income and capital gains in this reasonably valued equity.

J. P. Stevens

J. P. Stevens is a highly diversified manufacturer of quality textile products, operating 45 plants in the South and New England. Cotton goods account for the largest share of value, mostly in the form of finished articles for the industrial trade. Certain cotton items, for example Utica and Mohawk sheets and pillow cases, and other brand name items such as diapers, table cloths and tablet sets are manufactured and packaged for consumer sale.

While cotton fabrics are Stevens' prime manufacturing concern, synthetics run a close second, accounting for a little over one-third of volume. These are manufactured complete from purchased staple fibers and yarns to grey goods, and are sold primarily in the grey or unfinished state. In certain lines, however, synthetic fibers are carried through to the finished state and are sold principally for use as dress goods, underwear, suitings, sportswear

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drapery, industrial materials and in the automotive trade.

Woolens and worsted fabrics account for the remainder of volume. Virtually all of these are sold in the finished state, being used for a variety of cloths and underclothing. As with cotton and synthetic fibers, woolen and worsted fabrics are manufactured complete from purchased raw wool to finished goods, with the exception of a relatively small percentage of worsteds which are woven and finished by the company from yarn purchased from outside sources.

Stevens also acts as selling agent for other manufacturers in the merchandising of sheets, pillow cases, print cloths and fabrics made from spun rayon and other fibers. Many services are performed for these independent manufacturers, including styling, scheduling of promotion, assistance in quality control, testing and research assistance, market surveys, settlement of claims, assumption of credit risks, and maintenance of contracts with finishers.

Since 1946 J. P. Stevens has spent over $200 million in capital expenditures. A portion of this sum went toward the recent formation of a joint company with Kimberly-Clark, called Kimberly-Stevens, for the development and promotion of nonwoven materials. Although near-term earnings will not be affected by this operation, it should enhance the potential value of J. P. Stevens over the long term. This likewise holds true for other recent acquisitions, such as Borden Mills, a producer of quality print cloths, and Angle Silk Mills, a manufacturer of synthetic dress fabrics. All told, Stevens' expansion program has resulted in one of the most modern and efficient plant operations in the industry, enabling the company to increase its output and utilize more effectively personnel and resources.

Another valuable tool which should be considered in the long-term outlook for Stevens is its research department—the largest of any company in the textile field. One of the main problems of the industry is the constant introduction on the market of new fabrics to compete with already existing products. To keep abreast of competition, Stevens conducts continuing experiments in its plants on the newer man-made fibers to achieve better processing methods and new end uses. The development of totally new fabrics is also emphasized. In addition to the testing of materials in process and finished fabrics, problems of quality control are also studied by Stevens' researchers. Through new developments fostered by the department, the company should be

J. P. STEVENS

Recent Price	33⅜
Dividend	$1.50
Yield	4.5%
1959 Price Range	34⅜-26⅛
Traded	N.Y.S.E.

Capitalization (11/1/58)	
Long term debt	$57,600,000
Common stock	4,243,820 shs.

able to maintain its strong position in the trade for years ahead.

Stevens is also active in the field of market research, where it works to achieve wider distribution of goods through a greater knowledge of potential markets and to determine the degree of acceptance of a particular product. This program is rounded out by Stevens-sponsored research projects undertaken by several research institutions and textile schools.

Contrary to the rest of the textile industry, sales of J. P. Stevens have expanded rapidly, moving from $277.7 million in 1954 to $417.7 million in 1957. Poor economic conditions and high dealer inventories resulted in a decline in sales to a little over $386 million in 1958; but last year, with the company operating at nearly full capacity at most of its plants, sales topped $459 million. Accordingly earnings, during the 1954-58 period expanded from 90¢ to $2.60 a share, and for the fiscal year ended October 31, 1959, plant economies, rising demand and higher prices combined to push earnings to $4.52 a share, although part of these earnings were tax-free because of tax loss carryforwards of acquisitions. Continuance of strong demand for the company's products appears likely through at least the first half of 1960, and an increasing sales base, plus expected wider profit margins, could improve earnings still further this fiscal year. Since full taxes will be paid, however, after-tax earnings per share will show only a minor gain, if any. With this prospect in view, the present 37½¢ quarterly dividend will probably be increased or supplemented by extra cash payments.

Keeping in mind the above considerations, we believe that Stevens should prove attractive to buyers seeking capital appreciation over the intermediate term and who are willing to assume the risks of investing in the textile industry. With further improvement anticipated, shares of J. P. Stevens, selling at less than 8 times 1960 estimated earnings, appear undervalued.

James Lees & Sons

James Lees & Sons is the second largest producer of rugs and carpets in the United States, specializing in medium- and high-priced lines. The company is also the largest maker of carpet yarns, more than half of which go into its own products. Woolen rugs in velvet, axminster and wilton weaves have long been the mainstay of its line, but in recent years Lees has successfully introduced carpets made of synthetic fibers and of synthetics combined with wool.

Along with the rest of the carpet industry, Lees was hit by the economic recession which began in 1957 and continued through the first half of 1958. This circumstance, coupled with weakened demand for and lower prices on products—not to mention start-up expenses at several of its new southern facilities—resulted in a 1957 earnings decline to $3.82 from $4.86 in the previous year. Results for the first half of 1958 were even less encouraging, with earnings down 50% from previous year figures. However, the general business revival in the latter half of the year, together with an increase in the number of housing starts, prompted dealers to replenish depleted stocks, and by year-end 1958, earnings had rebounded sharply, totaling $4.04 for the full year.

While 1958 may be considered to have been a good year in that the company recovered from its earlier setback and reversed its earnings trend, indications are that when the final results of the year ended December 31, 1959, are made known, Lees will have posted the highest earnings in its history. Preliminary figures for the first nine months showed income of $4.09 a share—more than double the like 1958 period—and a figure of $5.65 seems a good possibility for the full year.

This remarkable improvement can be attributed to several factors. For one thing, during the past few years Lees has undertaken to terminate its manufacturing operations in the North and centralize all plant activities in southern locales. This program was completed in 1958, when operations of the last northern plant, in Bridgeport, Pennsylvania, were transferred to a new tufted carpet mill at Rabun Gap, Georgia. Thus, the cessation of Lees' activities in the North, plus the loss on property sales and the start-up expenses of southern operations, resulted in a considerable drain on revenue that were of a non-recurring nature. In addition to incurring extraordinary expenses through the localizing of plant operations in 1957, Lees also accelerated its program to modernize and expand existing plant and equipment. Capital ex-

Each of the babies pictured on this page was borne by a mother with a *documented* previous history of true habitual abortion, who was treated with DELALUTIN during the pregnancy leading to this birth

L VING PROOF OF FETAL SALVAGE WITH DELALUTIN

SQU BB HYDROXYPROGESTERONE CAPROATE

Improved Progestational Therapy

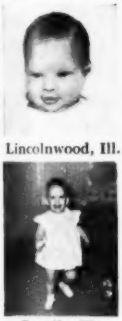
Garden City, N. Y.

Skokie, Ill.

Denver, Colo.

Denver, Colo.

No. Massapequa, L. I., N. Y.



Roselle, Ill.

Seaford, N. Y.

Hartford, Conn.

East Williston, N. Y.

Norwich, Vt.

DELALUTIN offers these advantages over other progestational agents

• long-acting sustained therapy • more effective in producing and maintaining a completely matured secretory endometrium • no androgenic effect • more concentrated solution requiring injection of less vehicle • unusually well-tolerated, even in large doses • fewer injections required • low viscosity makes administration easy

Complete information on administration and dosage is supplied in the package insert

Supply: Vials of 2 and 10 cc., each containing 125 mg. of hydroxyprogesterone caproate in benzyl benzoate and sesame oil.

SQUIBB *Squibb Quality - The Priceless Ingredient*

"DELALUTIN" ® IS A SQUIBB TRADEMARK

penditures that year were double the amount the company had expended during any previous single year of its operation. Of the $9.5 million spent in 1957, nearly 85% was used to build and equip three new plants in the South, which cost a total of $17 million.

However, now that the company's expansion program is nearing completion, expenditures of this nature are expected to drop to normal levels. Moreover, Lees is just now beginning to enjoy the benefits of its new facilities. As of late 1959, one of the three new plants was operating at full efficiency, and the other two are expected to reach top capacity during 1960. With these substantial additions to output, Lees should capture a greater percentage of the market in the coming year.

To maintain its position as one of the leaders in the carpet industry, Lees must, of necessity, maintain fully competitive research facilities. Recently, Lees designers have been greatly aided by the development of a new, exclusive wool scouring technique which gives an extra whiteness in wool blends that are to be dyed. Company researchers have also developed a permanent mothproofing compound which is added to all wool yarns used in carpets. Another important advance was the pioneering, with duPont of the first synthetic yarn designed specifically for use in carpets. Known as Nylon 501, the product was introduced commecrially early last year; response to the new carpets has been so enthusiastic that the company is being hard pressed to meet demand.

Looking to the 1960 fiscal year, the outlook for the carpet industry—and for Lees in particular—is encouraging. Although housing starts are expected to decline slightly, sales should equal, if not better, last year's. The trend of carpet wool prices has been upward, although this has been substantially offset by the increases in the selling prices of Lees' products. Further, even greater efficiency should be attained in the operations of the company's new facilities, enabling it to maintain its better-than-industry-average profit margins.

Over the past five years, dividens have averaged 50% of net, and the company has maintained a 50¢ quarterly rate. With earnings rising and the outlook bright, the $2.00 annual dividend may well well be supplemented by an extra cash payment—or a stock dividend may be paid in addition to the 50¢ quarterly, as was the case in 1959.

In the past, Lees has been able to outperform others in the highly volatile carpet trade; and considering the company's leadership

JAMES LEES & SONS

Recent Price	41½	Capitalization (12/31/58)	
Dividend	$2.00	Long-term debt	$12,394,999
Yield	4.8%	$3.85 Cum. Pfd.	
1959 Range Price	52½-39	($100 Par)	22,640 shs.
Traded	N.Y.S.E.	Common Stock	919,688 shs.*

*30% closely held.

in research, its outstanding merchandising methods and the benefits derived from its recent modernization and expansion, we believe they will continue to hold a top position in the industry.

The shares, selling at a little more than 7 times earnings and yielding approximately 5%, with a higher dividend in prospect, appear very reasonably priced for those seeking appreciation and income over the next year.◀

"COUGH...

one of the most frequent symptoms for which the patient seeks medical attention."[1]

SYNEPHRICOL®

ANTIHISTAMINIC • DECONGESTANT

Cough Syrup

...relieves the cough due to colds
...eases the allergic cough

●

Synephricol acts by prompt and prolonged decongestion of bronchial mucous membranes, by mild central sedation, and by decreasing sensitivity of the pharyngeal mucosa through antihistaminic action.

FORMULA:
(4 cc. teaspoonful)

Neo-Synephrine® hydrochloride	5.0 mg.
Thenfadil® hydrochloride	4.0 mg.
Dihydrocodeinone bitartrate*	1.33 mg.
Potassium guaiacol sulfonate	70.0 mg.
Ammonium chloride	70.0 mg.
Menthol	1.0 mg.
Chloroform	0.0166 cc.
Alcohol	8%

**Exempt narcotic*

DOSAGE:

Adults—1 or 2 teaspoonfuls every two to four hours, not to exceed 5 doses in twenty-four hours.
Children 6 to 12 years—½ to 1 teaspoonful four or five times daily.

BOTTLES OF 1 PINT AND 1 U. S. GALLON.

Winthrop LABORATORIES
NEW YORK 18, N. Y.

1. Banyai, A. L.: Management of Cough in Daily Practice, J.A.M.A., 148:501, Feb. 16, 1952.

Synephricol, Neo-Synephrine (brand of phenylephrine) and Thenfadil (brand of thenyldiamine), trademarks reg. U. S. Pat. Off.

▶Vitamin A & D Ointment with Prednisolone *(White)*

Prednisolone 0.5% plus the standard Vitamin A & D Ointment. *Indications:* For topical treatment of localized inflammatory skin conditions. For dermatitis due to thermal or chemical irritation, allergic dermatoses, contact dermatitis, atopic dermatitis, non specific pruritus and neurodermatitis. *Dosage:* A small quantity to be rubbed gently on the affected areas three or four times daily. Gauze dressing may be applied when indicated. *Supplied:* In 10 gram tubes or 25 gram tubes.

▶Durabolin *(Organon)*

Long-acting biologic stimulant. Each cc. contains 25 mg. of nandrolone phenpropionate in sterile sesame oil. *Indications:* Debility states, asthenia, anorexia, cachexia and weight loss; osteoporosis, ostenogenesis imperfecta and slowly-healing uncomplicated fractures; inoperable, estrogen-dependent mammary carcinoma; pre- and post-operatively; during corticosteroid therapy; severe trauma (third-degree burns, decubitus ulcers) and uremia. *Cautions:* Not recommended in congestive heart failure. Use with caution when the cardio-renal reserve is limited. Contraindicated in prostate cancer. *Dosage:* Adults, 25 mg. by intramuscular or subcutaneous injection once weekly, or 50 mg. every second week. Half these amounts are recommended for children over seven. *Supplied:* In 5 cc. multiple dose vials and 1 cc. (box of 3) ampuls.

► NeoDecadron 0.05% Ophthalmic Ointment *(Merck Sharp & Dohme)*

Dexamethasone 21-phosphate and neomycin sulfate in an ointment base. *Indications:* Allergic conjunctivitis, sty, granulating eyelids, pink eye, against inflammation due to chemical irritants and foreign bodies, contact dermatitis of the eyelids. In the treatment of superficial or deep keratitis or acne rosacea keratitis, mild, acute iritis, and ophthalmic herpes zoster (but not indicated for herpes simplex). *Dosage:* For topical administration. *Supplied:* In tubes containing 3.5 gm. of ointment.

Atarax Parenteral Solution *(Roerig)*

Each cc. of solution contains 50 mg. of hydroxyzine hydrochloride. *Indications:* Treatment of acutely disturbed or hysterical patients, various psychoses, chronic or acute alcoholism with anxiety, alcoholic withdrawal symptoms or delerium tremens and in any case not amenable to oral medication. *Dosage:* For deep intramuscular injection or intravenous injection. When given intravenously it should be injected slowly, at a rate of 1 cc. per minute. *Supplied:* In ampules containing 2 cc. of solution.

► **Ilosone Lauryl Sulfate 125 for Oral Suspension** *(Lilly)*

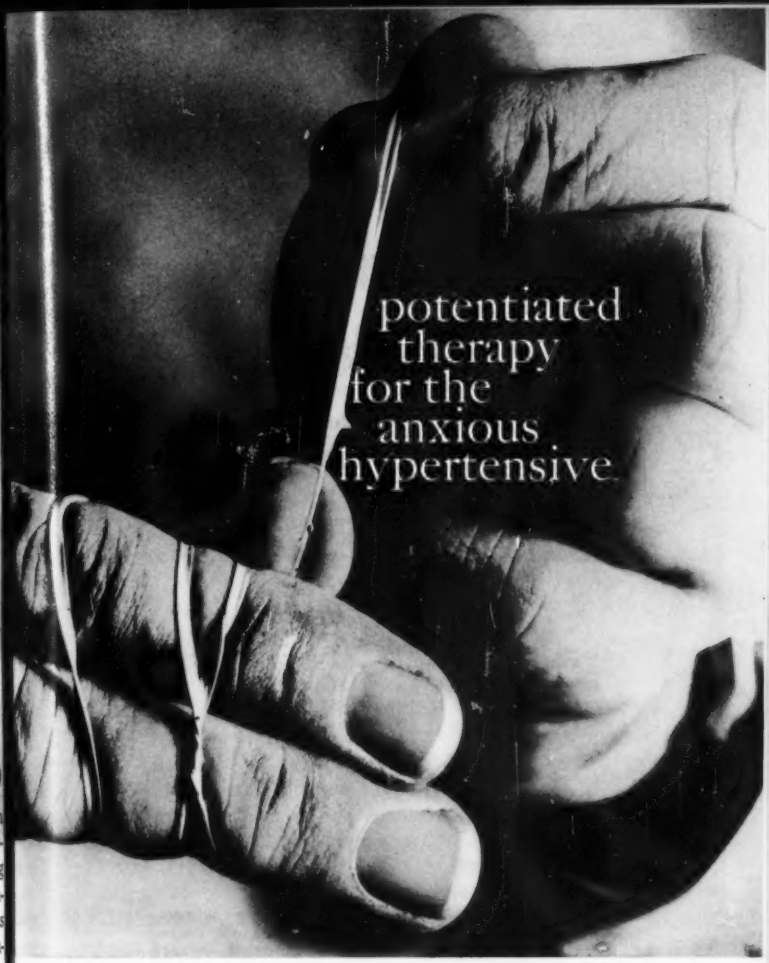
When water is added as directed, each 5 cc. of the resulting suspension will provide activity equivalent to that of 125 mg. of erythromycin base. *Indications:* For the treatment of most commonly encountered bacterial infections. Especially useful for the treatment of bacterial infections of the respiratory system and for a wide variety of infections caused primarily by staphylococci, streptococci and pneumococci. *Dosage:* Adults, 250 mg. every six hours. For more severe infections, 500 mg. every six hours. In overwhelming infections, 1 gm. every six hours. Children, according to weight of patient. *Supplied:* In a 60 cc. bottle containing the flavored granules of propionyl erythromycin lauryl sulfate to be mixed with water for oral suspension.

► **Decadron Phosphate 0.1% Topical Cream** *(Merck Sharp & Dohme)*

Dexamethasone 21-phosphate in a topical cream. *Indications:* As topical therapy in infantile eczema, atopic dermatitis, allergic eczema, housewives dermatitis, occupational dermatitis, seborrheic dermatitis and pruritus ani. *Dosage:* For topical administration. *Supplied:* In tubes containing 5 gm. or 15 gm. of the cream.

► **Decadron Phosphate 0.1% Ophthalmic Solution** *(Merck Sharp & Dohme)*

Dexamethasone 21-phosphate in true solution. *Indications:* Allergic conjunctivitis, sty, granulating eyelids, pink eye. Against inflammation due to chemical irritants and foreign bodies. In treating superficial or deep keratitis or acne rosacea keratitis, mild, acute iritis, and ophthalmic herpes zoster (but not indicated for herpes simplex). *Dosage:* For topical administration. *Supplied:* In dropper bottles containing 5 cc. of solution.



Serpasil®-Esidrix® gives anxiety-
dden hypertensive patients the pronounced central calming
tion they need while it brings their blood pressure down
lower levels than can usually be achieved with single-
ug therapy. And the antihypertensive effect is faster—
od pressure generally begins to fall within the first
w days of therapy. In addition, Serpasil-Esidrix controls
e tachycardia that often accompanies hypertension.

PPLIED: Serpasil-Esidrix *Tablets*, each
ntaining 0.1 mg. Serpasil and 25 mg. Esidrix.

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SUMMIT N. J.

PASIL®-ESIDRIX® (reserpine and hydrochlorothiazide CIBA)

► Difficult Diagnosis: A Guide to the Interpretation of Obscure Illness

by H. J. Roberts, M.D., formerly Research Fellow and Instructor in Medicine, Tufts University Medical School, and formerly Research Fellow and Instructor in Medicine, Georgetown Medical School. W. B. Saunders Company, Philadelphia & London. 1958. $19.00

Cases of serious illness which prove difficult to diagnose after careful history taking, examination, and all seemingly pertinent laboratory investigations, have on occasion vexed all physicians. It is to help practicing physicians in the solution of the problems presented by such cases that this book is presented. Some disease conditions of practically every nature and of any organ or system of organs fall into the category of extremely difficult diagnosis. Part 1 is devoted to groupings of related diseases frequently presenting puzzling illness, part 2 to classification and analysis of useful diagnostic procedures. Included among these procedures are therapeutic, diagnostic, withdrawal and provocative tests. An index of signs, symptoms and laboratory manifestations is appended for quick reference.

The purchase and use of this volume will enable the attending physician to diagnose and treat properly many patients who otherwise would have to be referred. The book fills a real and important need in the daily practice of medicine.

► Health in the Mexican-American Culture: A Community Study

by Margaret Clark, University of California Press, Berkeley & Los Angeles. 1959. $5.00

This study, conducted by a Committee of public-health and social-science specialists (funds being supplied by the Rosenberg Foundation), is an intensive investigation of a Mexican-United States community on the edge of San Jose, California. The detailed examination is of the social, economic, religious, and loric characteristics which have important bearing upon problems of health and disease. The rather complete report should be of great interest to public health authorities, all other physicians, students of government — indeed all intelligent persons.

reduces postnasal drainage — lessens pharyngeal irritation
depresses the cough reflex — eases expulsion of mucus

*The addition of the decongestant to the antitussive provides more complete cough control than regular "cough syrups". The central antitussive action of Dormethan[1] and the expectorant action of ammonium chloride are complemented by the decongestant action of Triaminic,[2, 3, 4] which reduces swelling and controls irritating postnasal drip, a common cough stimulus.

Each tsp. (5 ml.) of fruit-flavored, non-alcoholic TRIAMINICOL provides:

Triaminic ®	25 mg.
(phenylpropanolamine HCl	12.5 mg.
pheniramine maleate	6.25 mg.
pyrilamine maleate	6.25 mg.)
Dormethan	15 mg.
(brand of dextromethorphan HBr)	
Ammonium chloride	90 mg.

Dosage (to be administered every 3 or 4 hours): *Adults*—2 tsp.; *Children 6 to 12*—1 tsp.; *1 to 6*—½ tsp.; *under 1*—¼ tsp. One dose at bedtime is usually sufficient to control the cough cycle initiated by postural drainage of paranasal sinuses.

References: 1. Bickerman, H. A.: in Drugs of Choice, Mosby, St. Louis, 1958, p. 357. 2. Lhotka, F. M.: Illinois M. J. *112*:259 (Dec.) 1957. 3. Fabricant, N. D.: E.E.N.T. Monthly *37*:460 (July) 1958. 4. Farmer, D. F.: Cin. Med. *5*:1183 (Sept.) 1958.

Triaminicol®

the decontussive cough syrup

SMITH-DORSEY • a division of The Wander Company • Lincoln, Nebraska

► Autogenic Training: A Psychophysiologic Approach in Psychotherapy

by Johannes H. Schultz, M.D., and Wolfgang Luthe, M.D. Grune & Stratton, New York. 1959. $9.50

We are told that "in the course of his studies Oskar Vogt observed that intelligent and critical subjects could learn to induce certain 'autosuggestive states' by applying a sequence of autosuggestions patterned according to verbal approaches used during the induction phase of hypnosis." This will serve to give an idea of what is meant by Autogenic Training. The author expresses the wish that while reading through the different chapters his English-speaking colleagues will apply their critical judgment and thus get interested in the method.

► Physiology of Cardiac Surgery: The Beaumont Lecture, Wayne County Medical Society

by Frank Gollan, M.D., Assistant Director of Professional Service for Research Veterans Administration Hospital, Nashville. Charles C. Thomas, Springfield, Ill. 1959. $4.50

The opinion is expressed that surgeons may be blinded by the brilliant success of pioneers in this field and may be swayed from the course of strictly controlled experimentation. The anoxic tolerance of living tissue is the chief desideratum. Since hypothermia and extracorporeal circulation imply the intentional change from normal for a definite purpose, the induction of these conditions has intensely interested physiologists for a long time. No effort is made at an evaluation of equipment now available for these purposes, what is attempted is intelligent discussion of many unsolved physiological problems.

► That the Patient May Know

by Harry F. Dowling, M.D., Sc.D., Professor of Medicine, University of Illinois and Tom Jones, B.F.A., Professor of Medical Illustration (Emeritus), University of Illinois. Assisted by Virginia Samter. W. B. Saunders Company, Philadelphia & London. 1959. $7.50

Although not all books are fittingly named, this one is. While not subscribing to the often repeated statement that "one picture is worth a thousand words," the reviewer has no hesitancy in saying that the doctor who makes use of this book regularly will find it less and less difficult to enable his patients to know just what he is talking about, and why.

YESTERDAY, A COUGH SPOILED HIS DRAWIN

TODAY HIS COUGH IS UNDER CONTROL

WITH

BENYLIN®
EXPECTORANT

BENYLIN EXPECTORANT contains in each fluidounce:

Benadryl® hydrochloride (diphenhydramine hydrochloride, Parke-Davis)	80 mg.
Ammonium chloride	12 gr.
Sodium citrate	5 gr.
Chloroform	2 gr.
Menthol	1/10 gr.
Alcohol	5%

supplied: BENYLIN EXPECTORANT is available in 16-ounce and 1-gallon bottles.

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